CHILD HEALTH AND CHILD PSYCHIATRY
NEIGHBOURS OR COLLEAGUES? *

MILDRED CREAK
M.D. Lond., F.R.C.P., D.P.M.

PHYSICIAN IN PSYCHOLOGICAL MEDICINE,
THE HOSPITAL FOR SICK CHILDREN,
GREAT ORMOND STREET, LONDON, W.C.1

Charles West, who founded the Hospital for Sick Children, was pre-eminently a clinician, and his cases are described with great care. In one paper (1843) he describes 37 postmortem examinations, most of them performed by himself " unaided in the children's homes ". In his famous treatise of 1854 he points out that, of 50,000 persons dying annually in London, 20,000 were children under 10 years of age; and it is against this background of physical suffering in the early 19th century that one must consider his unusual and advanced views. What has particularly impressed me is his awareness of the part played by anxiety and mental unrest in the problems of the sick child. He saw anxiety and grief as actual factors in making and keeping a child ill, and he quotes more than one case in which emotional factors were the turning-point. In asking his students to engage in pædiatric study, he tells them: " Your old means of investigating disease will here to a great degree fail you, and you will feel almost as if you had to learn your alphabet again." He goes on to describe the language of signs given by a child; and by this he does not mean physical signs but those subtler reactions of byplay and concealment which can be so often used and directly exploited as a means of access to understanding an emotional problem. He puts it to the students that it is " as if you were to hear around you everywhere the sounds of a foreign tongue, and to observe manners and customs such as you had never seen before ". But, he adds, " if you are not fond of little children you cannot learn it, for they soon make up their minds as to who loves them, and when ill they will express their real feelings, whether by words or signs, to no one else ".

From Charles West's approach to children's medicine one can appreciate how far pædiatrics has travelled in the past hundred years and how far it still has to go. Recession of the tide of physical illness, and the measure of control we have acquired over infection, seem to have accentuated our need to understand the nervous child and his sickness, and the role of anxiety in the medical problems of today. West was aware of the sickness of both mind and body in his small patients: indeed, he did not separate these into two different aspects of practice. Here he was perhaps fortunate in not having a child psychiatrist to turn to. Just as we can imagine him learning more from his pains-taking postmortems in the lamplit room of one of his patients' homes than from any account of another man's examination of the same material, so he would need to find his own way of understanding the nervous child. Nowadays, it is true, he would be expected to know more of morbid anatomy than could possibly be extracted by his crude methods.

* * *

Yet were his methods, after all, so crude? Certainly he lacked the research tools which are, many of them, commonplace equipment today; but he made greater use of that human tool, the interview, than many a busy clinician who snatches time from reading off the results of investigations to glance at his living patient.

The interview is the basic tool of psychiatry. (For children who are too young to use words with facility or precision, active play, drawing and make-believe can be adapted to take its place.) The language of any person-to-person interview—not perhaps especially that of the doctor-patient interview—is by no means exactly what it seems. It is a language which must be learnt if it is to be understood. The doctor-patient interview will not only concern itself with facts but also seek to understand something of the fears and doubts which language often intends to conceal. In other words, all doctors need to become aware of the emotional factors which colour a patient's reaction to his illness. The psychiatrist's skill lies in adapting his interviewing techniques so that they shall give him as much of this information as they can. His art lies not only in uncovering defences but in conveying to the patients that he understands what they say, interpreting and reading back the record to them. Time-consuming, of course; but it was Charles West, who had never heard of Freud, who said " you must be most lavish of your time ".

Perhaps it is because the psychiatrist deals with ordinary knowledge, viewed differently, that he is so often mistaken for a particularly obscure and erudite person—or at worst a most peculiar kind of fool. In fact he should be one who throws new light on familiar situations and who does this rather by a shift of emphasis, and a new valency, than by any startling discoveries in fact. His task is to understand the more primitive feeling which lies behind the defences to which we all accustom ourselves, even quite early in childhood. A memorable sentence comes to mind from Prof. Walter Raleigh's essay on Style (1907). He is speaking of poets and their manner of saying what they have to say: " This blend of dignity and intimacy, of candour and self-respect is unintelligible to the vulgar, who understand by intimacy, mutual concession to a base ideal, and who are so accustomed to deal with masks, that when they see a face they are shocked as by some grotesque." And later, speaking of the generality of modern men and women who pretend to literature, he makes the very significant observation (in of course this entirely different context):

> " Their masks have for the most part grown to their faces, so that except in some rare animal paroxysm of emotion, it is hardly themselves that they express."

For the psychiatrist to be successful with his patients, especially when these are children, not only must he himself be able to shed his mask, but he must allow his patients to do so. How can he then convey the significance of this experience without running the risk of appearing either ridiculous or unintelligible, or both, to his safely masked colleagues? Must not our training of young men and women who are going to deal with sick children and their parents enable them to do just this—namely, to distinguish somewhat between the covering mask, and the face of primitive feeling?

Nowhere is the psychiatric approach more necessary than in the taking of the history, and in my view the essential art in history-taking lies in allowing both the

* From the Charles West lecture for 1958, delivered before the Royal College of Physicians of London on Nov. 18.

parent and the child to experience something of this unmasked reality in communication. Time has to be allowed for the building of some sort of relationship in order that this can happen. It has nothing whatever to do with the amassing of clinical facts, although a seemingly unimportant detail may often be startlingly emphasised, in much the same way that a familiar building is seen anew when floodlit against the night sky.

Also of great importance is the value placed on fantasy. Are we not at fault in seeking to distinguish between a "real" pain and an imaginary one? Fantasy is our own, and as such has an absolute validity in our personal life, whereas reality is something which happens to us. This apparently mischievous and irresponsible twisting of values is something which the psychiatrist must undertake if he is to make either his practice or his theory about it meaningful to his colleagues, and he steers a tricky course between naiveté and absurdity. But this he must do, without any concession to our normally accepted "masked" thinking, if he is to be both intelligible and significant to those whom he is teaching.

In all pædiatric hospitals—indeed in medicine generally—there is a growing awareness of this aspect of illness. Perhaps it is because we can no longer shelter behind the urgent need of getting sick patients well, and fending off death itself, that we are uneasily aware, as of a fog approaching, of the little-understood emotional factors. The fog will not be dispersed by forced ventilation into a newly opened department of psychological medicine. It is almost as if the more you know the more you see; and the more you see, the less you know—a sorcerer's apprentice kind of miasma.

* * *

Just to take a look at this, with the help of my colleagues at The Hospital for Sick Children, I invited the registrars who work in the medical outpatient department to grade their cases into three categories:

A. Those in which, so far as they could see, emotional factors played no part.

B. Those in which, though some well-defined physical abnormality was present, emotional factors helped maintain the symptoms.

C. Those in which the problem was mainly or entirely one of emotional disorder.

The cases were classified in this way after the first interview, as soon as the child and mother had been seen, and the forms were collected daily. While the investigation was going on, I interviewed each of the fifteen doctors concerned so as to find out what he (or she) thought about the scheme; whether it had raised any questions in his mind; and whether the results surprised him. At this interview I made a note of their qualifications, previous training, and experience, paying special attention to undergraduate (and any other) training in psychiatry.

The study extended over seven months, but records were not taken during two spells of influenza, which obviously altered the ordinary nature of the outpatient clientèle. The chart shows the percentage of cases assigned by each of the doctors to each of the three categories. The doctors are numbered 1–15 according to the (descending) percentage of cases they assigned to category A ("emotional factors played no part").

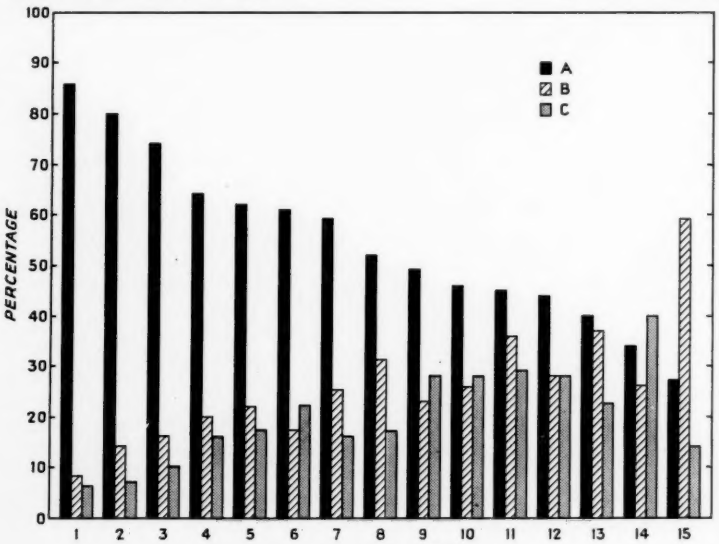
From such an informal and improvised inquiry, one must not try to extract more information than it will yield. But we may note that half these young doctors—who were pædiatricians not psychiatrists—believed that they were seeing rather more psychological than physical illness. They took this view even though the great majority of the children had been sent up as medical problems, and had parents who were sure that they were physically ill. We begin then to see something of the size of the problem.

What of the doctors facing it? Their psychiatric education had been gained before they graduated in medicine. What they had since learnt in practice was a great deal more important, as most of them realised; but none had ever held a psychiatric post or had any special postgraduate training in psychiatry.

Two doctors were older than the others, one having qualified in 1927 and the other in 1934, and they each did a single outpatient session a week. But their views were not essentially different from those of the younger people who were working through their registrarships.

Though one might suppose that medical teaching had been revolutionised in the twenty years between 1934 and 1954, the date of the most recently qualified, the teaching in psychiatry given to 7 of these 15 doctors was not essentially different from that given to the 1934 graduate. The 1927 graduate summarised the psychiatric education in her teaching hospital as "not a scrap", while a 1948 graduate spoke of his as "I might almost say none".

Their comments on the scheme itself were interesting, and none of them seemed surprised at the amount of emotional disorder they recorded. One point, made by several, was most



Summary of the results of the investigation.

The numbers of cases seen varied considerably and are here given as percentages. It will be seen that A=B+C (approximately) at doctor no. 8. Thereafter B+C>A, but never to the extent that A>B+C in those doctors to the left of the diagram. As far as could be judged, with the exception of doctor no. 3, who had a greater share of "casualty" cases than the others, the clinical material varied less than the doctors' opinion of it.

graphically expressed by a graduate who remarked on what had always been regarded as a " good teaching case " as being one with " good physical signs ". Since coming into practice he had become acutely aware of his failure to understand the case without such signs. He expressed himself as wanting an outpatient clinic " for the dross " —thus displaying both his wish to learn more about it, and his sense that such material is rejected.

* * *

We are thus brought to face a new aspect of pædiatrics. Nervous disorder in childhood is nothing new, as can be seen from the attention paid to it by Charles West and by many others who followed him, such as Guthrie (1907), Myers (1922), and Hector Cameron (1919). But its mounting claim to be recognised and successfully treated within the pædiatric field constitutes a demand which neither the pædiatricians nor the psychiatrists are yet in a position to meet. The situation could be described in a more challenging and a more political way by saying that here, clearly, is a job to be done, and nobody doing it. The pædiatrician, by and large, is not trained to do it; the child psychiatrist is not there in sufficient numbers to take it on, and he is usually not in the same place as the pædiatric material. On the rare occasions when he emerges from underneath his waiting-list, he may be able to take on a case or two; but to do this he must take it away from the pædiatric hospital where the parents feel that this sick child belongs. In painting this picture I am rather deliberately exaggerating the colours; but that there is a state of emergency I do not doubt. It is clearly not going to be overcome quickly, either by dramatic changes in the curriculum or by the unlikely introduction of additional consultant posts.

But in other ways, too, child psychiatry may be unready to meet the challenge coming from pædiatricians.

As a specialty child psychiatry was officially " born " in this country when the first trainees were sent to clinics in the U.S.A. by the Commonwealth Fund of America in 1928. The first child-guidance clinic had been started just before this, in 1926; so the growth of this particular service has been both rapid and recent. In a memorandum on the training of the consultant child psychiatrist, issued in 1951, the child psychiatry section of the Royal Medico-Psychological Association calculated the needs of the country as something like 400 clinics, each with a psychiatrist giving full-time service: this estimate was based on Blacker's (1946) view that 1–2% of all children are likely to need psychiatric help during their school life. The number of child-guidance clinics in England and Wales in 1950 was quoted as about 150. In a further memorandum from the same source, on the provision of psychiatric services for children and adolescents, issued in 1955, it was stated that the number of clinics had risen to 196, but not all had full-time psychiatric services. In the 1958 edition of the directory of the National Association for Mental Health, about 350 clinics are listed for England and Wales; but by no means all have a full psychiatric service, and many have vacancies among the staff. Though this shows that the growth between 1951 and 1955 has been exceeded by the growth between 1955 and 1958, the number still falls short of a need calculated as long ago as 1946—and for schoolchildren only. We know that in fact a very great many problems emerge in the preschool years—the problems of feeding and of sleep and other habit regulation, the problems of early separation and severe jealousies. Since these can often be best solved within the family setting, long before the child reaches school age, it is clear that even the new growth of clinics is not going to be able to meet the demands upon it.

* * *

My fear is that psychiatry may fail to meet the challenge of pædiatrics at three levels, all interrelated. Firstly, some child psychiatrists are neither mature nor experienced enough to take their place as consultants in their own specialty, and secondly there are not enough of them. With an overall shortage, people have been appointed sometimes with inadequate training, but more often seriously lacking experience in this field. Hardly has a man finished training before he finds himself the only applicant for the post of directing a clinic which is already probably short of a psychiatric social worker. He may be miles from a hospital, and out of contact with the pædiatrician for the area, with whom he has no common meeting-place. He will spend many hours travelling from one to the other clinic in his area; he will have little or no time to treat his own cases, and must therefore either dispose of them to a school for maladjusted children, or relegate them to a lay therapist working in his clinic. Since the therapist will know the case, and he himself will no longer do so unless their contact is intimate and their team-work really well organised (a technique he has had no time to learn or practise, apart from his short training), he will find himself doing little more than rubber-stamping other people's decisions. His sense of being always overworked may in part derive from this situation—namely, that of never really seeing a case through to a satisfactory result. In this setting he is unlikely to do really good work. Nor is he able at all to consider original research, reading the results of other's work, or systematic study and publication of his own. He may be further isolated by being, on the terms of his appointment, a senior hospital medical officer working under a principal school medical officer who likes to deal in figures and results. And the only impressive figures our wretched man has to present are those of his waiting-list. This is admittedly to exaggerate many of today's difficulties, since they are not necessarily all present in every case. But for many potentially able child psychiatrists the picture is not overdrawn.

* * *

Have we given due thought to this factor of the rapid emergence of child psychiatry during an epoch in which the patterns of psychiatric knowledge as a whole have so greatly altered? Child psychiatry has passed through infancy: it has just and no more passed its 11-plus, admitting it to the ranks of respectable specialisation, only to be faced with the torments of growing up, unsure of its tenets, and uneasy in its loyalties. One might almost think of it as the child of a broken marriage between orthodox psychiatry and psychoanalysis. This fanciful simile comes to my mind alongside the memory of an adolescent patient who, faced with the situation of divorced parents for both of whom she felt deeply, said, " I feel as if I had come to where the road divides and I don't know which way to go." Her temporary solution was a schizophrenic breakdown, landing her in a distressing period of mental chaos from which she eventually made a good recovery. In considering the future of child psychiatry it seems important to look at some of these relevant factors, so as to avoid both the breakdown and any sort of malevolence and mudslinging in the way of a

divorce. It may even seem as though a little too much has been expected of us.

With his special gift for stating profound truths in a disarmingly simple way, Winnicott (1958) has shown how the adult personality is inextricably grown from the roots of infancy, and points out that psychoanalysts spend much time helping their adult patients to rediscover the primitive and infantile self, so that, by reliving these earlier conflicts, they may understand to what an extent these can account for difficulties in the present. This practice is based on recognition and acceptance of unconscious mental processes; and in child analysis the language of fantasy is the key to this world. I need not elaborate Winnicott's lucid explanation given of the need for analytic training, and the experience of a personal analysis, for those pædiatricians who are going to deal with the psychological problems in childhood. While the practical difficulties are immense, the far greater difficulty lies in accepting their necessity.

I spoke earlier of the increasing divergence between adult psychiatry and psychoanalysis. In one way this is more apparent than real, and has been due to vigorous growth at both ends of a continuum. The position of the patient in a mental hospital has been completely transformed by the newer forms of *physical* treatment; yet the mental hospitals have probably never had so many keen young psychiatrists who have been, or are being, analysed. Many feel that the vogue for active physical treatment does not take the patient far enough and that the " electricians " have lost sight of their patients' human problems. In spite of all this activity, and acceptance of mental treatment as something very different from custodial care, the hospital population of those who are chronically ill remains about the same. Although the open-door policy, group therapy, remedial occupation, and sedation, combined with physical treatment from time to time, may have transformed their lives, they remain mentally ill. Thus, the registrar in training as a psychiatrist in the mental hospital will have plenty to do, but much of it will seem remote from the kind of work required from the child psychiatrist.

On the other hand, the simple investigation I have described suggests that the pædiatrician is already meeting, and trying to solve, problems he would like help with from the psychiatrist. Where he should look for this help, and whether he can get it, depends on several factors. If orthodox psychiatry and psychoanalysis are divorced, may not pædiatrics fill the role of third party? Where is the child psychiatrist to look either for education or, when educated, for a place to practise in?

* * *

Children have always had their periods of disturbed behaviour; and when Charles West spoke of such defects as " moral " he was in a sense labelling them as something outside his sphere, for which he need not feel directly responsible. On the other hand, he made it clear that these so-called moral problems must be reckoned with in any disturbance affecting the health or welfare of his child patients.

Nowadays, it almost seems as though there were no limit to the areas over which psychiatry in childhood may expect to exert an influence. Certainly most of us would include juvenile delinquency, remedial education, and that awful bulging and expanding ragbag, psychosomatic medicine; also infant-welfare clinics, schools for physically handicapped children, and perhaps homes and orphanages. If that were not enough, we could include the newer difficulties thrown up by migrant populations and refugee camps. The area of suffering childhood a hundred years ago was perhaps as large numerically; but, as medical progress has shown, the problem was simpler, and capable of an unexpectedly swift solution. Problems similar to our own of the 19th century still exist in many developing areas, as Cicely Williams (1958) has lately reminded us; but at least what should be done for their solution is known. Can we say that with equal confidence of our own —even if we limit ourselves to neurosis in childhood? Certainly we cannot do so if we include psychosomatic ills and today's problem of the increase in juvenile acts of aggression. If we are no longer clear about *what* should be done, it is indeed difficult to know who is to do it, and where.

* * *

Such doubts link closely with what I see as the third way in which psychiatry may fail to meet the pædiatricians' needs: they may find they do not talk the same language. This language needs to be learnt, as Pasmore (1958) has said in an article about psychiatry and general practice. But Charles West said something very like that in his description of the children's physician attuning himself to what his patient is trying to tell him: his words were " almost as if you had to learn your alphabet again ". So it will already have been part of the pædiatrician's training to learn the language of childhood. This is not the same as the language of the unconscious, which makes such free use of fantasy; and though they certainly have points in common, Winnicott (1958) remarks that this study of psychological factors by the pædiatrician is not just a matter of " being good with children ": it asks of the doctor who practises it no less than a fundamentally new approach. This is something of which many pædiatricians are now aware, even if they do not at once appreciate what it may mean to them in time, money, personal effort, and often personal inquietude. This they will come to realise as they acquire the training they need in order to specialise in child psychiatry and particularly so in child analysis.

Need the language barrier be so great? If the student could take his child psychiatry in his training, and if he learned something of the art of interviewing throughout his clinical years, would not his undergraduate experience of child psychiatry and pædiatric medicine blend to the advance of his understanding of both subjects? This experience would have to include case-taking, personal contact with both children and parents, and perhaps with their homes, with the rest of the family, and with the school. Some of the most interesting experiments in medical education have been built around the awareness that the patient, whatever his age and whatever his complaint, is a whole person seen in a social setting.

This point of view seems to me quite indispensable in understanding a child, who remains for so long relatively dependent on the family matrix. Even if his complaint is as objective as a broken leg, his recovery can be hastened or retarded by his home circumstances. The pædiatrician does not, of course, require a psychiatrist to tell him that. But it would seem as though defensive attitudes, shutting off that awareness, often begin during the difficult years of clinical study; and it is when this happens that the divergence of approach crystallises into what I have called a different language. It might seem as if I pleaded that only the psychiatrists were party to the truth. On the contrary, I believe that they too may suffer from mental

isolation, and that the study of the mental mechanisms of the sick child can be evaluated only alongside the experience of watching him in his illness. Each discipline has much to learn from the other, so long as they can communicate.

This might also tend towards a better, more natural, selection of psychiatrists. At present it requires a particular effort on the part of the student to spend an adequate amount of time in psychiatric departments. Those who make the effort seem to be often the highbrows and the odd ones in the group. As I learned from the registrars who helped in the outpatient inquiry, it is only later, when they have worked at first hand and singlehanded with their patients, that they want to know more about how to handle the material which they now recognise as being so prolifically psychiatric in its scope. Some of these are men and women who might have found great satisfaction in the practice of psychiatry. Such self-selection of psychiatrists might bring the supply nearer in line to the demand, with psychiatry less an esoteric subject, and no longer isolated from the rest of medicine. At least the reverse is known to be true—that many feel profoundly dissatisfied at confining themselves to a narrow organically minded approach. A very few, likely to be always a minority, have sought a personal analysis in order to equip themselves better for their job, which will still be as pædiatricians. Winnicott puts it forward as the method of choice for those pædiatricians who hope to practise psychiatry in this field. In these and in other ways pædiatricians are most urgently requesting both clinical help and training from their psychiatric colleagues. It is an invitation in the terms of a challenge. The great danger lies in failing to see what the challenge involves in reshaping the child psychiatric services, and in the challenger—I mean the pædiatrician—not knowing enough to see what he is asking.

* * *

In conclusion, there seems no escape from taking another look at the curriculum. This is no more than was done in a memorandum of the Royal College of Physicians on the teaching of psychiatry, issued in 1943. This has still to be fully implemented.

Undergraduate training must at least familiarise the student with patterns of normal physical and emotional development, so that he can be alerted to the abnormal, when he meets it in his clinical years. His first-hand contact with psychiatric patients of all ages must be enough to give him a basis for handling problems. The art of interviewing could become a neglected art in a practice which owes so much to increasingly complex techniques of investigation.

For the student, this early familiarity would have the double effect of allowing a normal sensitiveness to human problems to develop pari passu with some means of handling them. Otherwise he runs the danger of over-identification with the patient.

The opposite danger is that a hearty denial of the existence of psychological illness will end as a mask that obscures the living face of human emotion.

Somehow a place, in the geographical sense, must be found for psychiatric work with children—in the children's hospitals. The clinic or the child-guidance centre which has no physical liaison with the other pædiatric services will be lost to them, and will itself lose much. Correspondence and even the telephone are no substitute for the means whereby a problem, or the case itself, may be jointly seen and discussed.

I wonder, too, whether the very real difficulty of teaching psychiatry on the job—that is, by apprenticeship—has not been somewhat exaggerated. A recent article (Davies et al. 1958) suggests that students can handle cases, given close enough supervision and the opportunity for conference.

This will all inevitably involve fresh thinking about the training of the child psychiatrist. Some pædiatricians will elect to train themselves for this work by means of a personal analysis; but probably only a few will come into it by this route. Others, perhaps at the registrar stage, will elect to take a more orthodox training, including adult psychiatry, neurology, and mental deficiency. To make this workable there must be an acceptable framework of opportunity for satisfying practice, within a reasonable span of time.

It will be a bad day for medicine when learning by apprenticeship is superseded by a succession of courses. But the success of the apprenticeship depends quite as much on time in which to teach as it does on time for learning. Above all, both the pupil and the teacher have to perfect this essentially human art of communication with their patients and with each other. Their apprenticeship, as in all medicine, is to truth.

REFERENCES

Blacker, C. P. (1946) Neurosis and the Mental Health Services. London.
Cameron, H. C. (1919) The Nervous Child. London.
Davies, E. T. L., Davies, T. T., O'Neill, D. (1958) *Lancet*, ii, 34.
Guthrie, L. (1907) Functional Nervous Disorders in Childhood. London.
Myers, B. (1922) Practical Handbook of the Diseases of Children. London.
Pasmore, H. S. (1958) *Lancet*, i, 524.
Raleigh, W. (1907) Style. London.
Royal College of Physicians (1943) Committee on Psychological Medicine. Interim Report on Undergraduate Education in Psychiatry.
West, C. (1843) *Brit. for. med. Rev.* **15**, 543.
— (1854) How to Nurse Sick Children. London.
— (1854) Lectures on the Diseases of Infancy and Childhood. London.
— (1860) *Med. Times, Lond.* **20**, 133.
— (1871) Lumleian Lectures on some Disorders of the Nervous System in Childhood. London.
— (1877) Medical pamphlets. Letter to the governors of the Hospital for Sick Children, London.
Williams, C. (1958) *Lancet*, i, 863, 919.
Winnicott, D. W. (1958) Modern Trends in Pædiatrics (edited by A. Holzel and P. J. M. Tizard). London.

BLOOD-SUGAR RESPONSE OF NORMAL ADULTS TO DEXTROSE, SUCROSE, AND LIQUID GLUCOSE

Sir CHARLES DODDS
M.V.O., M.D. Lond., F.R.C.P., F.R.S.
COURTAULD PROFESSOR OF BIOCHEMISTRY

F. A. FAIRWEATHER
M.B. Lond.
ASSISTANT PATHOLOGIST, BLAND-SUTTON INSTITUTE OF PATHOLOGY

A. L. MILLER
M.B. Lond.
LECTURER IN CHEMICAL PATHOLOGY

C. F. M. ROSE
A.R.I.C.
CLINICAL BIOCHEMIST

From the Courtauld Institute of Biochemistry, Middlesex Hospital, London, W.1

THERE has been recent renewed interest in the relative merits of dextrose and sucrose as sources of carbohydrate. It has been claimed that, as dextrose is the sugar normally found in the blood in the postabsorptive state, whereas sucrose must be hydrolysed by invertase to dextrose and fructose prior to absorption, the administration of dextrose is the most natural and efficient way of supplying

readily available carbohydrate. As a consequence of this assumption, dextrose and dextrose drinks have been employed therapeutically, particularly in the management of febrile patients in whom the metabolic rate is increased as a result of the increased body-temperature and in whom an adequate calorie intake is often difficult to maintain owing to nausea and anorexia.

In 1925 Bennett and Dodds showed that large quantities of liquid glucose could be administered to such patients and to patients suffering from malnutrition, with considerable therapeutic advantage. They stressed particularly that this substance is relatively less sweet than sucrose and is, therefore, better tolerated by both normal and anorexic subjects.

Higgins (1916) showed that the respiratory quotient rose more rapidly after the oral administration of sucrose than after dextrose, and this was confirmed by Deuel (1927). These findings suggested more rapid metabolic utilisation of sucrose. There was, however, no information in this work that the rise in respiratory quotient after sucrose indicated metabolism of the absorbed hexoses in the peripheral tissues, such as muscle. It was indeed suggested that it was probably due to metabolism of fructose by the liver.

Rabinowitch (1945) followed the blood-sugar level at minute intervals following the ingestion of sucrose by mildly hypoglycæmic diabetic subjects, and showed that a significant rise occurred within 5 minutes in each of ten patients. No comparable experiment involving the administration of dextrose to such patients has been carried out.

TABLE I—BLOOD-SUGAR (MG. PER 100 ML.) BY METHOD OF FOLIN AND WU

Subject No.	Sex	Sugar	Time (min)								
			F	2	5	10	15	30	60	90	120
1	M	D	100	100	135	138	143	136	139	100	89
		S	100	105	129	144	141	95	112	90	95
		LG	97	107	129	132	158	159	118	82	93
2	M	D	88	94	97	100	119	121	67	69	84
		S	93	95	98	115	127	103	81	85	87
		LG	86	91	90	91	105	115	85	80	82
3	M	D	90	84	89	116	129	94	89	80	80
		S	95	93	97	118	128	112	68	82	79
		LG	93	92	104	115	144	103	71	86	85
4	M	D	89	87	94	109	125	104	86	69	85
		S	92	90	90	109	128	133	72	69	69
		LG	97	91	94	112	112	94	75	59	77
5	M	D	78	95	95	110	115	131	125	87	83
		S	83	67	74	86	102	136	95	79	62
		LG	87	102	100	110	123	138	110	69	77
6	M	D	98	95	102	133	143	138	92	88	88
		S	92	84	89	97	103	123	105	73	91
		LG	100	100	120	139	153	133	105	81	81
7	F	D	81	81	107	116	139	120	92	94	79
		S	91	89	..	100	124	128	79	73	81
		LG	75	89	89	113	..	148	134	65	59
8	M	D	94	97	97	97	103	137	127	106	79
		S	94	80	91	100	118	132	88	85	82
		LG	84	92	95	95	100	118	116	95	82
9	F	D	98	100	97	107	112	133	139	88	79
		S	87	95	98	100	137	132	110	116	80
		LG	95	97	103	115	120	144	138	77	64
10	F	D	94	91	91	106	112	103	85	97	91
		S	88	88	94	121	106	115	88	91	94
		LG	94	94	92	103	111	100	81	72	75
11	M	D	102	95	101	131	140	140	88	81	..
		S	93	86	96	105	119	162	93	68	..
		LG	75	90	85	91	100	154	77	72	72
12	F	D	90	80	80	89	108	102	88	76	..
		S	86	86	84	116	128	92	68	80	84
		LG	84	76	94	106	133	114	86	76	88
13	M	D	94	101	96	100	110	132	76	74	..
		S	91	96	97	95	101	124	111	68	..
		LG	86	88	96	105	124	113	86	78	82
14	M	D	92	90	90	104	125	117	78	82	..
		S	88	86	93	104	122	123	88	74	..
		LG	68	68	80	92	127	80	68	75	75

D = dextrose. S = sucrose. LG = liquid glucose. F = fasting.

TABLE II—BLOOD-SUGAR LEVELS (MG. PER 100 ML.) IN 5 SUBJECTS BY METHOD OF FOLIN AND WU

Subject no.	Sex	Sugar	Time (min.)								
			F	2	5	9	14	20	30	60	90
A	M	D	98	98	134	140	145	147	114	125	82
		S	88	102	104	131	150	173	150	96	64
		LG	96	93	102	111	128	123	126	105	74
B	F	D	89	95	98	107	116	121	129	109	86
		S	95	91	102	104	130	121	96	63	68
		LG	88	91	99	122	109	94	89	88	104
C	F	D	106	92	97	124	128	140	110	95	65
		S	88	84	88	100	107	123	103	58	75
		LG	86	88	97	97	107	110	102	74	82
D	F	D	97	99	103	119	113	103	99	99	79
		S	97	92	100	106	110	103	100	73	92
		LG	88	88	97	106	112	97	87	87	83
E	F	D	100	97	106	115	134	151	164	122	103
		S	94	91	97	95	125	122	100	96	72
		LG	91	90	96	118	128	130	124	97	86

Abbreviations as in table I.

In the course of work in this field, it was decided to study the blood-sugar response of healthy young subjects (aged 22–26) to equivalent doses of three common carbohydrate substances—dextrose, sucrose, and liquid glucose—with particular reference to the rise in blood-sugar in the early minutes of the experiment. Liquid glucose was included because this preparation is used in a number of popular proprietary glucose drinks. It is a viscid syrup prepared by the enzymatic hydrolysis of cereal starches. The liquid glucose used was *B.P.* 1953 except for being slightly more dilute (78·5% w/w carbohydrate solids). The dextrose equivalent was 42·5; and, from the data published by the Technical Advisory Bureau, Corn Industries Research Foundation (1956), the liquid glucose was calculated to contain approximately (% w/w): dextrose 14·8, disaccharides (mainly maltose) 11·0, higher oligosaccharides (tri- to hepta-saccharides) 33·2, dextrins (octa- and higher saccharides) 19·4.

The purpose of this paper is to present the results obtained in this study. It is clear that studies on blood-sugar levels can only have indirect relevance to the problem of the clinical usefulness of carbohydrates, since the important issue in this matter is the availability of readily utilisable sugars to peripheral tissues, such as muscle and brain. For this reason, no attempt will be made to attach any clinical significance to the findings reported.

Method

In a first series, fourteen subjects (ten males and four females) were examined. After fasting overnight, a blood sample was taken for determination of the fasting blood-sugar. The subjects were then given the carbohydrate substance under investigation dissolved in 250 ml. of water, and this they drank as quickly as possible, usually within a minute. The amounts of the three " sugars " used were such that the dose of each represented a carbohydrate intake of 45·4 g. Thus 50 g. of dextrose monohydrate, 45·4 g. of sucrose, and 56·8 g. of liquid glucose were administered. Blood samples, obtained by venepuncture, were taken at 2, 5, 10, 15, 30, 60, 90, and 120 minutes after the subject completed the ingestion of the sugar.

Each subject attended on three occasions within a week, receiving a different carbohydrate on each occasion. Samples of urine obtained at 1 and 2 hours were examined for reducing substances, but no glycosuria occurred in any subject. Blood-sugar determinations were carried out using a modified Folin and Wu technique.

In a second series of tests, a further five subjects (four female and one male) were examined using a similar method. The only difference was that blood samples were taken 2, 5, 9, 14, 20, 30, 60, and 90 minutes after ingestion of the sugar

TABLE III—BLOOD-SUGAR LEVELS (MG. PER 100 ML.) BY GLUCOSE-OXIDASE METHOD

Subject no.	Sex	Sugar	Time (min.) F	2	5	9	14	20	30	60	90
A	M	D	76	89	105	119	128	125	90	107	59
		S	82	85	85	115	122	142	122	87	47
		LG	79	81	96	101	121	115	118	95	57
B	F	D	73	..	73	93	101	107	113	97	65
		S	83	76	103	142	112	125	133	50	61
		LG	77	75	83	102	98	77	79	78	74
C	F	D	73	80	87	107	105	122	101	83	60
		S	76	73	70	87	95	102	92	49	50
		LG	77	76	92	92	100	106	93	70	75
D	F	D	70	75	83	92	95	86	90	75	43
		S	85	76	87	86	94	103	80	80	62
		LG	73	75	85	86	93	86	72	82	73
E	F	D	73	93	95	100	108	137	150	106	93
		S	62	69	81	120	121	108	80	68	57
		LG	75	75	85	103	112	120	116	82	64

Abbreviations as in table I.

so that six specimens were obtained in the first 30 minutes instead of five as in the previous series. Blood-sugar determinations were carried out by the Folin and Wu technique as before, but in addition "true glucose" determinations were done by the glucose oxidase method described by Huggett and Nixon (1957).

In the two series of tests, therefore, tolerance curves after the three substances have been followed in nineteen normal subjects—eleven male and eight female.

Results and Discussion

The results of blood-sugar determinations on nineteen subjects using the Folin and Wu method are shown in tables I and II, and the blood-glucose results obtained by the glucose oxidase method in five subjects are shown in table III.

After the administration of all three substances the blood-sugar rises rapidly. In fig. 1 the mean times taken for (*a*) a 10% rise and (*b*) a 10 mg. per 100 ml. rise in blood-sugar above the fasting level to occur after the administration of the three sugars are compared. In obtaining these results, the time taken was determined by noting the point on the plotted blood-sugar curve representing the appropriate increase and reading off the corresponding time from the graph. This assumes that the rise in blood-sugar occurred at a uniform rate between any two points on the curve—which is probably a valid assumption, as the time intervals involved are short. The results show that by either method of analysis, the mean time required for a significant rise in blood-sugar is greatest after sucrose and least after liquid glucose, dextrose occupying an intermediate position. The difference between the times for liquid glucose and sucrose is satistically significant ($P = 0.02$).

Rabinowitch (1945) also used a 10 mg. per 100 ml. rise as his criterion for a significant increase in blood-sugar, and the mean time taken for this to occur in his ten subjects was 2·8 minutes—which is considerably faster than the mean for any sugar in our subjects. This presumably reflects the well-recognised avidity of the hypoglycæmic subject for sugar.

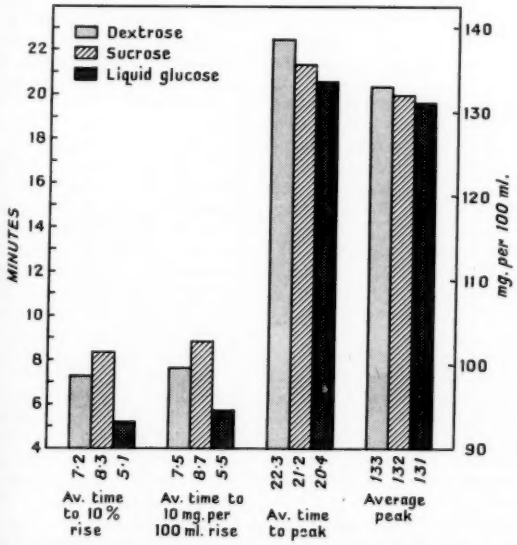


Fig. 1—Observations on blood-sugar levels after ingestion of dextrose, sucrose, and liquid glucose: average time taken for 10% rise; average time taken for rise of 10 mg. per 100 ml.; average time taken to reach peak; average peak blood-sugar level.

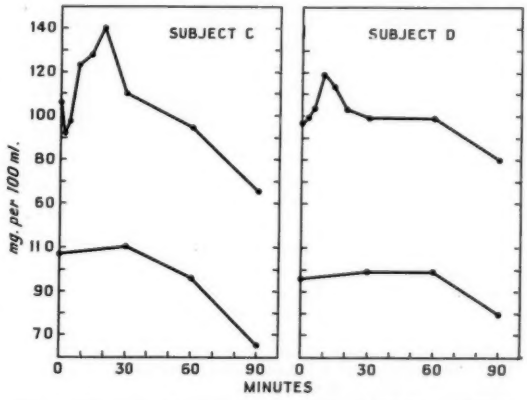


Fig. 2—Dextrose-tolerance curves (method of Folin and Wu).

Fig. 1 also compares the mean times taken for the peak blood-sugar level to be achieved and the mean heights of these peaks. There is no significant difference between the three substances in these respects, the peak level—some 40 mg. per 100 ml. above the fasting value—being reached in about 20 minutes. The rapidity with which the peak is reached is of some interest in that it is commonly stated that in the normal subject the maximum rise occurs between 30 and 60 minutes after the administration of a single dose of dextrose. In the standard procedure used for diagnostic glucose-tolerance tests in most hospitals, blood samples are taken fasting and at 30, 60, 90, and 120 minutes. The present results would suggest that this technique will miss the peak blood-sugar level in many normal young adults, and may even give a very misleading picture of glucose tolerance. This is clearly demonstrated in fig. 2, in which the dextrose-tolerance curves obtained in two subjects in the present experiments are compared with the curves which are obtained if only the blood-sugars taken at the standard glucose-tolerance-test times are plotted. In each case the standard time curve misses the peak level, and indeed shows virtually no rise in blood-sugar. It is, therefore, suggested that a fifteen-minute blood-sugar value should be obtained when diagnostic glucose-tolerance tests are carried out, at least in the case of young subjects in whom impaired absorption with a flat curve is anticipated.

The results on the five subjects who had blood-sugar determinations done by both the Folin and Wu and the glucose-oxidase method show clearly that the rise in blood-sugar is due predominantly to glucose, no matter which carbohydrate is administered. Values for non-glucose reducing substances can be calculated by taking the difference between the Folin and Wu and glucose-oxidase blood-sugar figures. Theoretically, if the entire rise in blood-sugar is due to glucose, this difference might be expected to remain constant. Fig. 3 shows mean non-glucose reducing substance curves derived from the five subjects. The curves obtained after the administration of dextrose and liquid glucose do not rise significantly above the fasting level at any time during the period of the

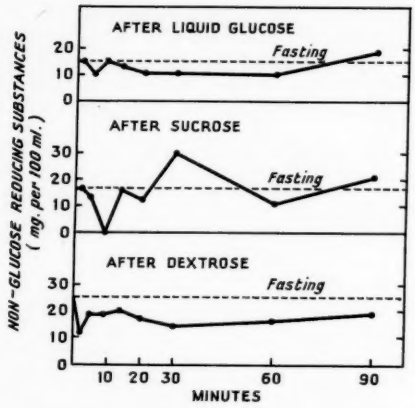


Fig. 3—Calculated non-glucose reducing substances: average curves obtained from 5 subjects after administration of liquid glucose, sucrose, and dextrose.

experiment. After sucrose, however, there is appreciable rise above the fasting level at 30 minutes, with a fall back to below the resting value at 60 minutes. The number of subjects investigated is too small to conclude that this is a constant or significant finding. If there is a definite increase in the non-glucose reducing substances in the blood after the administration of sucrose, a possible explanation would be the appearance of absorbed fructose unchanged in the systemic venous blood. There is, at the moment, no information on blood-fructose levels after the administration of sucrose, but further work along these lines is proceeding.

Conclusions and Summary

The blood-sugar response to amounts of dextrose, sucrose, and liquid glucose equivalent to 45·4 g. of carbohydrate has been followed in nineteen subjects.

All these carbohydrates were rapidly absorbed and produced a rapid rise in blood-sugar to a maximum which usually was reached within 30 minutes.

The importance of this observation in relation to diagnostic glucose-tolerance tests is discussed. The technique commonly used will miss the peak blood-sugar level in some young normal subjects and thus result in a misleading flat curve.

Liquid glucose produced a more rapid rise than sucrose (difference significant at $P=0.02$). The rise in the blood-sugar was predominantly due to glucose, no matter which carbohydrate was administered. There was, however, some evidence that the amount of non-glucose reducing substances in the blood increased after sucrose, but further work is required.

REFERENCES

Bennett, L. I., Dodds, E. C. (1925) *Lancet*, i, 429.
Deuel, H. J., Jr. (1927) *J. biol. Chem.* **75**, 367.
Higgins, H. L. (1916) *Amer. J. Physiol.* **41**, 258.
Huggett, A. St. G., Nixon, D. A. (1957) *Lancet*, ii, 368.
Rabinowitch, I. M. (1945) *J. Nutr.* **29**, 99.
Technical Advisory Bureau, Corn Industries Research Foundation (1956) *Mfg Confect.* **36**, 24.

CONGENITAL ADRENAL HYPOPLASIA IN SIBLINGS

R. G. MITCHELL
M.D. Edin., F.R.C.P.E., D.C.H.
CONSULTANT PÆDIATRICIAN, MARYFIELD HOSPITAL, DUNDEE

K. RHANEY
M.B. Edin., M.R.C.P.E.
SENIOR LECTURER IN CHILD HEALTH, UNIVERSITY OF ST. ANDREWS

ADRENAL insufficiency in early infancy is usually associated with hyperplasia of the adrenal glands—a well-recognised condition with a high familial incidence. Symptoms of insufficiency may, however, be due to hypoplasia of the adrenals, an anomaly which has rarely been reported except in association with anencephaly. No report has been found of a familial incidence of adrenal hypoplasia unaccompanied by other congenital malformations. We therefore report this in two brothers, the first of whom died at 8 weeks of age and was examined at necropsy, whereas the second has been maintained in good health by substitution therapy.

Case-reports

Case 1.—A firstborn male infant weighing 7 lb. 12 oz. (3·5 kg.), was born as a vertex delivery on Dec. 22, 1954. The mother was healthy and there was nothing significant in the family history. The pregnancy had been normal apart from vaginal moniliasis during the last three months. Fœtal distress occurred during labour and the head was delivered by forceps. The infant was in good condition at birth, was breast-fed, and gained weight rapidly until he was 3 weeks old by which time he weighed 9 lb. (4·1 kg.). He then began to vomit, at first once a day but gradually more often. His stools were normal and he continued to suck, although not so vigorously, and his mother was not unduly worried about his progress. But at 6 weeks of age he was found to weigh only 6 lb. 14 oz. (3·1 kg.) and was therefore admitted to hospital (Feb. 4, 1955).

On examination he was apathetic, poorly nourished, and slightly dehydrated. No other abnormality was found. He vomited immediately after several feeds, during which vigorous peristalsis was seen but a pyloric tumour was not palpated. Radiological examination showed no evidence of pyloric stenosis; he was therefore kept under observation and 0·45% saline solution was administered parenterally. As the vomiting and visible peristalsis persisted, an exploratory laparotomy was carried out (Feb. 7, 1955) but no abnormality was found. Postoperatively the level of plasma-chloride was 103 mEq. per litre and of bicarbonate 14·5 mEq. per litre. Half-strength Hartmann's solution containing dextrose was given intravenously, and during the next 36 hours the infant's condition improved. Thereafter unexpected deterioration occurred suddenly, with severe vomiting and collapse, and at this stage a diagnosis of adrenal insufficiency was first considered. This diagnosis could not be confirmed, for biochemical investigation of the blood showed plasma sodium to be 140 mEq. per litre, potassium 4·7 mEq. per litre, chloride 97 mEq. per litre, and bicarbonate 17·2 mEq. per litre. Intravenous therapy was continued with 1/6 molar sodium lactate followed by Hartmann's solution, and although no additional therapy was given the infant was much better by the next day (Feb. 10). The intravenous drip was stopped on Feb. 11, and for the

next 48 hours the infant fed well and gained weight; but on Feb. 13 his condition again suddenly deteriorated and he became grey and collapsed. No cause for this relapse was found; the urine was normal and the leucocyte-count was 10,400 per c.mm. Death occurred before further intravenous therapy could be effective and before sufficient urine could be collected for the estimation of 17-ketosteroids.

Fig 1—Case 1: hypoplastic adrenal (inset) compared with normal adrenal.

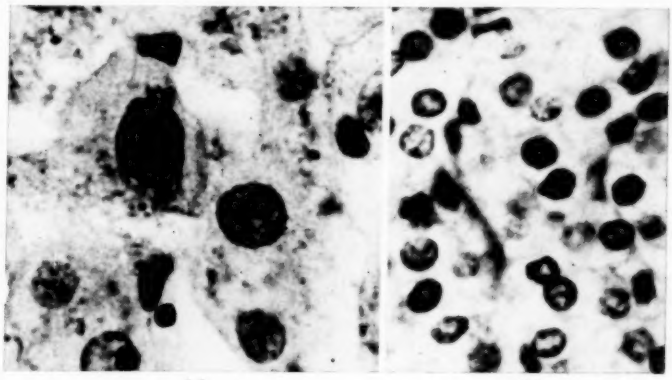


Fig. 3a—Case 1: giant cells in hypoplastic adrenal cortex (hæmatoxylin and eosin. × 1025).

Fig. 3b—Normal adrenal cortex at 6 weeks (hæmatoxylin and eosin. × 1025).

Necropsy

External examination.—The body was poorly nourished, weighing 6 lb. 13 oz. (3·1 kg.). The external genitalia were normal, and there was no pigmentation of the skin. The laparotomy incision had healed.

Internal examination.—This revealed adrenal hypoplasia as the only apparent cause of the infant's illness and death. The adrenal glands were extremely small (fig. 1), and their combined weight was 0·72 g. (the normal range at this age, according to Tähkä (1951), is 1·63–8·25 g.). They were slightly darker than usual, but they were of normal shape. The pituitary and thyroid glands and the pancreas were of normal size, shape, and appearance but unfortunately were not weighed. The thymus and spleen seemed slightly enlarged, but the lymph-nodes were not obviously abnormal.

The cardiovascular, respiratory, alimentary, genitourinary, and central nervous systems appeared to be normal.

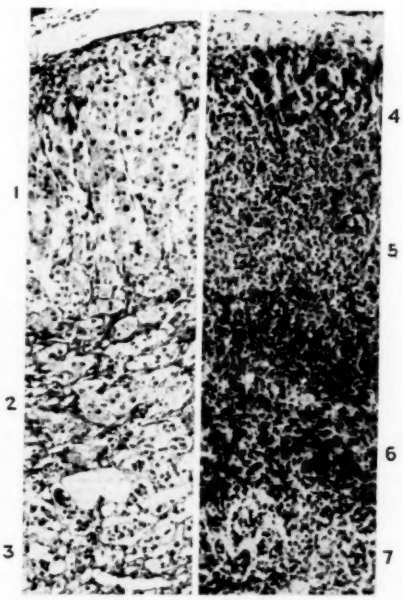


Fig. 2a—Case 1: hypoplastic adrenal showing (1) cortex composed of abnormal, large cells; (2) zone of atrophy and fibrosis; and (3) normal medulla (hæmatoxylin and van Gelson. × 150).

Fig. 2b—Normal adrenal cortex of an infant, aged 6 weeks, showing (4) zona glomerulosa, (5) zona fasciculata, (6) involuting fœtal cortex, and (7) medulla (hæmatoxylin and eosin. × 95).

Histology

Adrenal glands.—Both cortex and medulla are present; but, while the medulla is apparently normal, the cortex presents a very unusual appearance. The hypoplastic cortex contains very few cells (figs. 2a and 3a), but most of them are remarkably large and the width of the cortex appears approximately normal (fig. 2b). Furthermore, the usual cortical pattern is absent; the cells appear to be all of the same kind and show no differentiation into a zona glomerulosa and a zona fasciculata. The cells are loosely and irregularly arranged in trabeculæ between sinuses of varied width and are separated from the medulla by a zone of involution and fibrosis.

Most of the cortical cells have abundant eosinophilic cytoplasm and large nuclei. They are pleomorphic, and, though many of them appear to be completely detached from neighbouring cells, others are grouped together and have indefinite margins so that it is difficult to determine whether some of them are multinucleated. Many of the nuclei are large and vesicular and contain one, or even two, prominent nucleoli; others are dense, solid, and hyperchromatic, and some, situated chiefly in the inner part of the cortex, are undergoing degeneration. Mitotic figures are absent. The cytoplasm contains prominent granules which stain with hæmatoxylin but are Feulgen-negative. In some of the cells the granules are clustered together but in others they are dispersed throughout the cytoplasm or arranged in a circle near the periphery. Small vacuoles are present near some of the granules, but no eosinophilic inclusions have been found. Scharlach R shows that many cells in all parts of the cortex contain a little lipid.

Degenerative changes, such as loss of the nucleus and lysis of the cytoplasm, are most plentiful in the inner cortex; and a zone of atrophic cells and debris with condensation of the stroma occupies the same position as the involuting fœtal cortex in a normal adrenal gland. This zone contains a small amount of hæmosiderin, but there is no evidence that hæmorrhage has contributed to the adrenal abnormality.

The pituitary gland.—The anterior lobe appears normal. Unfortunately the gland was not sectioned horizontally, and therefore only an approximate differential cell-count could be made; but in a total count of nearly 8000 cells the proportions of acidophils and basophils fell within the normal range given by Rasmussen (1950).

No abnormality was seen in heart, lung, liver, spleen, pancreas, kidney, thyroid, testis, thymus, lymph-nodes, rib, intestine, or brain.

Fig. 4a—Case 2: the infant aged 4 weeks.

Fig. 4b—Case 2: the infant aged 6 months.

Case 2.—Three years after the death of her first infant, the mother gave birth to a second child, a boy, whose birth-weight was 8 lb. 4 oz. (3·8 kg.). Pregnancy and labour were normal, and the infant was born spontaneously by the vertex on Feb. 22, 1958. His condition at birth was good, his progress was satisfactory, and he had nearly regained his birth-weight when he left hospital on the 6th day. Unfortunately, the function of the adrenal glands was not investigated because the baby was born in a different hospital where the significance of the first infant's death was not appreciated.

At 15 days the infant weighed only 7 lb. 10 oz. (3·5 kg.), and complementary feeding was advised. At 3 weeks he began to vomit after feeds, became easily tired, and sucked weakly. He came under our observation when he was 25 days old (March 19), and was then found to be thin and slightly dehydrated, with greyish pallor and an anxious expression (fig. 4a). There was no pigmentation of the skin or other abnormality.

On admission to hospital, biochemical investigation gave the following results: plasma sodium 115 mEq. per litre, potassium 8·8 mEq. per litre, chloride 79 mEq. per litre, and bicarbonate 22·7 mEq. per litre. As these findings indicated severe adrenal insufficiency, the infant was treated with saline solution subcutaneously and orally while the nature of the adrenal defect was being investigated further. During the first week after admission, the blood-urea was 38 mg. per 100 ml., plasma-calcium 10·8 mg. per 100 ml., hæmoglobin 12·7 g. per 100 ml. and leucocytes 7000 per c.mm. Random blood-sugar determinations varied between 36 and 60 mg. per 100 ml. The urine contained no albumin, sugar, or cells. An electrocardiogram was normal on two occasions, although the plasma-potassium levels at these times were 8·9 and 9·4 mEq. per litre. Routine culture of the stool on admission grew a pathogenic *Escherichia coli* (O 26); and, although there was no diarrhœa, a course of chloramphenicol was given.

Further investigation.—Adrenal cortical activity and the response to corticotrophin were investigated over a period of five days (March 19–23) and the results are shown in the accompanying table. Unfortunately, the infant's general condition made it necessary to give small doses of adrenocortical hormones during the test and only one control observation could be made. Nevertheless, these necessary modifications are not considered to have influenced the results materially.

Diagnosis.—A presumptive diagnosis of adrenal hypoplasia was made in view of the obvious similarity of this infant's illness to that of his brother; it was confirmed, we believe, by the persistently high levels of potassium in the plasma and the low levels of 17-ketosteroids in the urine.

Treatment with 9-α-fluorohydrocortisone ('Fludrocortisone', Squibb) was started on March 22. The infant was also given additional sodium chloride (2 g. daily) in his feeds and small doses of cortisone acetate. Until the optimum dosage of these hormones was determined, occasional injections of deoxycortone acetate were given to keep the plasma-potassium level within safe limits. The amounts of hormones given during the five weeks which the infant spent in hospital, and the changes in plasma-electrolyte levels, body-weight, and systolic blood-pressure (estimated by the flush method) are shown in fig. 5. Eosinophil-counts and estimations of the urinary chloride excretion were made daily but were found to be of no value as a guide to progress or therapy. The eosinophil-count varied from 91 to 177 per c.mm., but was slightly lower while the infant was having corticotrophin (mean count 45 per c.mm.); the urinary chloride excretion varied between 4 and 14 g. per litre.

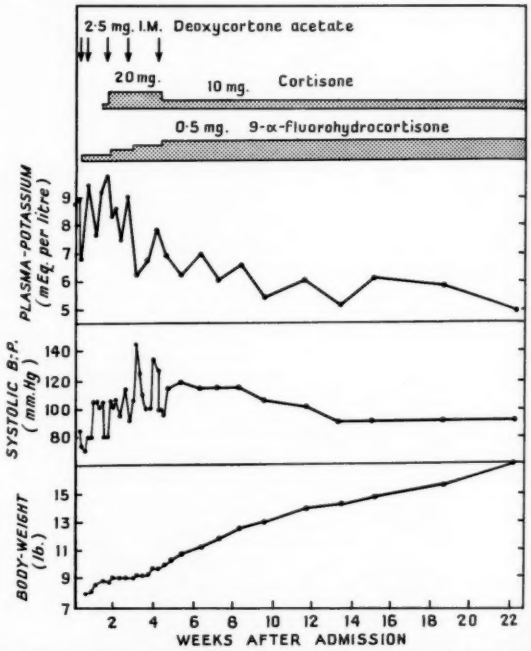


Fig. 5—Case 2: dosage of hormones used in treatment, and changes in plasma-potassium, systolic blood-pressure and body-weight.

The infant was discharged from hospital on April 22, on a maintenance dose of 9-α-fluorohydrocortisone 0·5 mg. daily in a single dose and cortisone acetate 5 mg. twice daily, with additional sodium chloride (2 g. daily) in his feeds. He has made good progress since then, and now at the age of 6 months weighs 17 lb. (7·7 kg.) and appears to be a normal healthy baby (fig. 4b). For the first three months after discharge satisfactory control was ensured by weekly determinations

CASE 2: EXCRETION OF 17-KETOSTEROIDS AND 17-KETOGENIC STEROIDS IN THE URINE BEFORE, DURING, AND AFTER INJECTION OF CORTICOTROPHIN

Day	Urine volume (ml.)	Urinary creatinine (mg. per 24 hr.)	Urinary 17-ketosteroids (mg. per 24 hr.)	Urinary 17-ketogenic steroids (mg. per 24 hr.)	Corticotrophin 10 units i.m. twice daily	Deoxycortone acetate 2·5 mg. i.m.	9-α-fluorohydrocortisone 0·2 mg. orally
1	236	24·5	0·24	2·91	Nil	Nil	Nil
2	345	43·5	0·40	5·90	+	Nil	Nil
3	150	22·5	0·23	3·42	+	+	Nil
4	254	35·6	0·17	3·18	+	Nil	+
5	240	39·1	0·19	2·91	Nil	Nil	+

17-ketosteroids and 17-ketogenic steroids were determined by the method of Norymberski et al. (1953) as modified in the indirect method by Sobel et al. (1958).

of plasma-electrolytes and blood-pressure (see fig. 5), but thereafter he was seen at longer intervals. It has not proved necessary to increase the maintenance doses of hormones or sodium chloride, but neither has it been possible to reduce them.

Discussion

Hypoplastic adrenal glands are most commonly associated with anencephaly. They have also been observed in infants who had congenital hypoplasia of the pituitary gland (Blizzard and Alberts 1956, Mosier 1956, Brewer 1957, Ehrlich 1957). In a few reported cases infants had congenital adrenal hypoplasia but no other congenital abnormalities.

Some of these infants lived for several weeks (Sikl 1948, Provenzano 1950, Williams and Robinson 1956 [cases 3 and 4], Harlem and Myhre 1957), and a few on replacement therapy survived for some months (Deamer and Silver 1950 [case 1], Geppert et al. 1950, MacMahon et al. 1957). They showed such features of adrenocortical insufficiency as vomiting, weakness, and recurrent electrolyte disturbances, and, in some, pigmentation of the skin. Though a few of the infants made poor progress from birth, most of them did not develop the characteristic symptoms until about the 3rd week of life. So far all the infants, except case 4 of Williams and Robinson (1956), have been males. The reference by Roberts (1949) to adrenal hypoplasia in three siblings is misleading, for, in a subsequent report of what is apparently the same family, the pathological findings clearly indicate that two of the infants had adrenal hyperplasia (Roberts and Baehren 1952).

A diagnosis of familial adrenal hypoplasia can be proved only at necropsy. Nevertheless, we believe that the combination of clinical and pathological evidence in our two cases strongly suggests that this rare condition sometimes has a familial incidence. In our first case, there was clinical evidence of adrenocortical insufficiency and the diagnosis of hypoplasia was established at necropsy when the combined weight of the adrenal glands (0·72 g.) was found to be considerably below the lower limit of the normal range. Thus, when the brother also developed symptoms of adrenal insufficiency with characteristic changes in electrolyte levels, a presumptive diagnosis of familial adrenal hypoplasia was made.

The additional investigations carried out on the surviving infant provide further evidence in favour of our diagnosis, although we recognise that none of them can be regarded as wholly conclusive.

Thus, the low level of 17-ketosteroids in the urine suggests hypoplasia rather than hyperplasia, for at this age infants with hyperplasia usually excrete excessive amounts. Furthermore, the values obtained for 17-ketogenic steroids in the urine are also compatible with this diagnosis, and may in fact be unduly high, since with the method used (see table) the Zimmermann reaction showed a large quantity of an interfering chromogen. Finally, the lack of response to corticotrophin, indicated by the absence of a significant increase in urinary steroids, is suggestive but not diagnostic of hypoplasia, for normal infants may also appear insensitive (Gottfried et al. 1957); and this finding does not entirely exclude hyperplasia, since in this condition the usual response to corticotrophin may not always occur (Prout and Snaith 1958).

Other causes of adrenocortical insufficiency in the newborn without excess androgen production have obviously to be considered in our second case. The condition might conceivably have been caused by hæmorrhage at birth (Williams and Robinson 1956, Wilkins 1957) or by congenital cysts (Moore and Cermak 1950), but when one infant is known to have died from adrenal hypoplasia, and there is nothing in the brother's history to suggest a different ætiology, it seems reasonable to diagnose familial adrenal hypoplasia.

The histological appearances in adrenal hyoplasia, as reported in the literature, show considerable variation. The histological appearances of the adrenal glands in our case seem to be identical with those described by Sikl (1948), MacMahon et al. (1957), and Harlem and Myhre (1957). In none of these cases was a lesion found in the pituitary gland, and in the adrenals the cortical cells were abnormally large and irregularly arranged without differentiation into glomerular and fasciculate zones. We agree with MacMahon et al. (1957) that the appearance is completely different from that in anencephaly, and that the abnormal cortical cells resemble the giant cells described by Kampmeier (1927) as occurring occasionally in the fœtal adrenal cortex. The histological picture also differs from that described in association with hypoplasia of the pituitary gland. The ætiology of the giant cells in the fœtal adrenal cortex is unknown (Potter 1952), and we can offer no suggestion as to their pathogenesis. Furthermore, we can throw no fresh light on the ætiology of congenital adrenal hypoplasia.

Treatment

The generally accepted treatment of adrenocortical insufficiency in infants has been based primarily on experience with the adrenogenital syndrome. In this condition cortisone is used to suppress overproduction of androgens; and deoxycortone acetate by injection or implantation, with additional sodium chloride, is given to correct the electrolyte disturbance (Wilkins 1957). In adrenal hypoplasia, however, the clinical picture is one of adrenocortical insufficiency without excessive formation of androgens, and therefore substitution therapy alone is required.

In case 2, the most important requirement was to restore and maintain electrolyte equilibrium, and for this purpose we used 9-α-fluorohydrocortisone orally in a single daily dose, and additional sodium chloride in the feeds. As the low levels of blood-sugar indicated impaired gluconeogenesis as well as mineralocorticoid deficiency, cortisone in small doses was also given.

When used in the treatment of infants with the adrenogenital syndrome, 9-α-fluorohydrocortisone in doses greater than 0·5 mg. daily has sometimes been found to cause serious hypertension (Owen et al. 1957, Wilkins 1957), and even with the smaller dose which we employed there was a temporary rise of systolic blood-pressure above the normal level while the dosage was being adjusted. On maintenance dosage, however, the blood-pressure has remained within the normal range and the therapy chosen would appear to have been justified by the infant's excellent progress and general well-being.

The severity of the clinical disturbance and of the electrolyte imbalance lead us to believe that the hypoplastic adrenal cortex produces little if any sodium-retaining hormone. Unfortunately, in our second case further investigation of the adrenal cortex, and in particular its response to stimulation, was precluded by the precarious condition of the infant. Furthermore, we have felt it unjustifiable to attempt further investigation of the adrenal cortical function at present, because fatalities may occur if the treatment of such infants is temporarily interrupted (Provenzano 1950).

Summary

In two brothers with adrenocortical insufficiency vomiting, dehydration, and weakness appeared at about 3 weeks after birth.

The firstborn died after repeated episodes of collapse and was found at necropsy to have adrenal hypoplasia unaccompanied by any other congenital abnormality.

His brother, born three years later, responded to treatment with 9-α-fluorohydrocortisone and cortisone, which corrected the severe electrolyte disturbance. Familial adrenal hypoplasia was diagnosed in view of the biochemical findings and the findings in the first case.

The hypoplastic adrenal cortex of the first infant consisted of abnormally large cells resembling the giant cells occasionally found in the fœtal adrenal cortex. The histological appearance was completely different from that found in association with anencephaly and with pituitary hypoplasia.

We thank Prof. J. L. Henderson and Prof. A. C. Lendrum for advice and criticisms; Dr. F. L. Mitchell, principal biochemist to Maryfield Hospital, for his generous help and for the biochemical investigations in case 2; and Mr. R. Fawkes for the histological preparations and photomicrographs.

REFERENCES

Blizzard, R. M., Alberts, M. (1956) *J. Pediat.* **48,** 782.
Brewer, D. B. (1957) *J. Path. Bact.* **73,** 59.
Deamer, W. C., Silver, H. K. (1950) *J. Pediat.* **37,** 490.
Ehrlich, R. M. (1957) *ibid.* **51,** 377.
Geppert, L. J., Spencer, W. A., Richmond, A. M. (1950) *ibid.* **37,** 1.
Gottfried, S. P., Bogin, M., Levycky, N. V. (1957) *ibid.* **50,** 170.
Harlem, O. K., Myhre, E. (1957) *A.M.A.J. Dis. Child.* **94,** 696.
Kampmeier, O. F. (1927) *Anat. Rec.* **37,** 95.
MacMahon, H. E., Wagner, R., Weiner, D. B. (1957) *A.M.A.J. Dis. Child.* **94,** 282.
Moore, F. P., Cermak, E. G. (1950) *J. Pediat.* **36,** 91.
Mosier, H. D. (1956) *ibid.* **48,** 633.
Norymberski, J. K., Stubbs, R. D., West, H. F. (1953) *Lancet,* i, 1276.
Owen, J. A., Engel, F. L., Wester, T. B. (1957) *J. clin. Endocrin.* **17,** 272.
Potter, E. L. (1952) Pathology of the Fetus and the Newborn. Chicago.
Prout, M., Snaith, A. H. (1958) *Arch. Dis. Childh.* **33,** 301.
Provenzano, R. W. (1950) *New Engl. J. Med.* **242,** 87.
Rasmussen, A. T. (1950) *Amer. J. Anat.* **86,** 75.
Roberts, M. H. (1949) *J. Amer. med. Ass.* **139,** 439.
— Baehren, P. F. (1952) *J. med. Ass. Georgia,* **41,** 299.
Sikl, H. (1948) *J. Path. Bact.* **60,** 323.
Sobel, C., Golub, O. J., Henry, R. J., Jacobs, S. L., Basu, G. K. (1958) *J. clin. Endocrin.* **18,** 208.
Tähkä, H. (1951) *Acta pædiat., Stockh.* suppl. 81.
Wilkins, L. (1957) The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence. Springfield.
Williams, A., Robinson, M. J. (1956) *Arch. Dis. Childh.* **31,** 265.

Addendum

Case 2.—At $11^1/_2$ months the infant is in good health on treatment with 9-α-fluorohydrocortisone 0·4 mg. once daily and cortisone acetate 5·0 mg. twice daily. He weighs 22 lb.; plasma-electrolyte levels and blood-pressure are within normal limits.

CIGARETTE SMOKING, SERUM-CHOLESTEROL, BLOOD-PRESSURE, AND BODY FATNESS

OBSERVATIONS IN FINLAND

MARTTI KARVONEN
M.D. Helsinki, Ph.D. Cantab.

ESKO ORMA
M.D. Helsinki

ANCEL KEYS
M.A., Ph.D. California, Ph.D. Cantab.

FLAMINIO FIDANZA *
M.D. Naples

JOSEF BROZEK
Ph.D. Prague

From the Institute of Occupational Health, Helsinki, Finland, and the Laboratory of Physiological Hygiene, University of Minnesota, Minneapolis, U.S.A.

WITHIN populations of the Western cultural pattern both retrospective and prospective studies show substantially higher mortality-rates among cigarette smokers than among non-smokers. To some extent the excess mortality among smokers is proportional to the intensity of smoking (Doll and Hill 1956, Hammond and Horn 1958a). Many ascribed causes of death contribute, but a large part of the total difference is attributed to ischæmic heart-disease among smokers (Hammond and Horn 1958b).

In the absence of evidence that habitual cigarette smoking directly accelerates atherogenesis or increases susceptibility to thrombosis, argument as to whether there is a cause-and-effect relationship between smoking and ischæmic heart-disease is speculative. In any event, it is pertinent to inquire whether smokers tend to differ from non-smokers in characteristics other than the smoking habit, especially those known or widely believed to be related to the development of ischæmic heart-disease. Such characteristics are the serum-cholesterol level, the arterial blood-pressure, and relative obesity or body fatness. In this paper we report the measurement of these variables in smokers and non-smokers from samples of the male population of Finland. Finland is of particular interest because of the high frequency of ischæmic heart-disease, particularly in East Finland (Keys et al. 1958).

Population Samples

The data we report are from an epidemiological study made in the late summer and autumn of 1956. This was at first concentrated on men in rural areas of East and West Finland, but was later expanded to include men of the Helsinki fire department, and business and professional men in Helsinki.

In both rural areas a number of small communities were selected to represent the Finnish countryside. Within these the local public-health nurses selected men aged 20–59, excluding Civil Servants, temporary residents, and those known to be ill. Very few refused to take part, and those initially reluctant usually sought appointments after the survey team had worked in the area for a few days. Those who did not present themselves were individually approached. The only difficulty was the pressure of non-invited volunteers who wanted to be included. These were not accepted except when it was expedient because of local public relations. The records of such volunteers were not included with those of the sample proper, nor were the records of those with dietary peculiarities, clinical evidence of cardiac or thyroid disease, subjective symptoms suggesting cardiac disease, or physical disabilities.

In both East and West Finland most of the men were farmers or timber workers, though less active occupations were also represented—e.g., car drivers, mechanics, and shopkeepers. The samples studied were thought to be representative of the men of their ages in the two areas concerned. This was not necessarily true of the Helsinki sample. About half of these men were regular members of the Helsinki fire department, and were representative of that group which in Helsinki, as in fire-brigades elsewhere, have a somewhat specialised mode of life. The remainder of the Helsinki sample was comprised of business and professional men, largely recruited from the members of the Helsinki Rotary Club, and an appreciable degree of self-selection was involved.

Methods

The men were asked to report for examination in the morning without breakfast, but no instructions were given about smoking before the start of the examination.

The examination included medical and dietary history, 9-lead electrocardiogram, body measurements, blood-sample, physical examination, and questions on past and present smoking habits. The questions were asked personally by a physician, and were similar to those used by the American Cancer Society (Hammond and Horn 1954).

Serum total-cholesterol was measured in duplicate as previously described (Anderson and Keys 1956). In both East and West Finland, two 0·1 ml. samples of serum were dried on filterpaper and sent to the laboratory in Minneapolis for analysis. In Helsinki this procedure was used and, in addition, the fresh serum was analysed at the Helsinki Institute of

* Present address: Istituto di Fisiologia Umana, Universita di Napoli, Naples, Italy.

Occupational Health.[1] Agreement between measurements on the fresh and the dried samples was satisfactory, as in our previous experience in such comparisons.

Blood-pressure was measured with a sphygmomanometer after the completion of the interview and questionnaire, while the subject remained seated. Diastolic pressure was recorded as the Korotkoff sounds finally disappeared.

Body fatness was estimated from the thickness of the skinfold measured under constant pressure, as recommended by the Committee on Nutritional Anthropometry (1956). The sum of the skinfolds over the triceps muscle and over the tip of the scapula was taken as the measure of fatness.

Smoking Habits

For the present purpose, attention is concentrated on the regular cigarette smokers and on the men who had never smoked regularly.

The numbers of men in the pipe, cigar, and "occasional smoking" classifications were too few for statistical analysis. The "stopped smoking" group was discarded because it was heterogeneous, including men who had stopped only a few weeks or months previously as well as those who had not smoked for more than 30 years.

In Finland two kinds of cigarettes were smoked at the time of the survey. The commonest was an American-type cigarette without a filter, 7 cm. long, 8 mm. in diameter, and containing about 1·2 g. of tobacco resembling the usual American blend. The second, Finnish-type cigarette contained only 0·45 g. of tobacco; the cigarette proper was 4 cm. long and 6·5 mm. in diameter, and was attached to a paper-tube mouthpiece 3·7 cm. long containing a small loose cotton-wool filter.

TABLE I—REGULAR CIGARETTE SMOKERS AND NON-SMOKERS

	West Finland	*East Finland*	*Helsinki*
No. of smokers:	91	103	166
Smoking Finnish-type cigarettes	57%	31%	16%
Smoking over 20 cigarettes daily	25%	42%	15%
No. of non-smokers	64	39	62
Ratio of smokers/non-smokers	1·42	2·64	2·68

The average tobacco consumption was highest in East Finland (table I). The ratio of smokers/non-smokers was similar in East Finland and in Helsinki, but was much lower in West Finland. The percentage of heavy smokers (over 20 cigarettes daily) was much higher in East Finland. This fact, as well as other differences between the samples, made a separate comparison of the smokers and non-smokers of each region desirable. For the final statistical analysis we used the method of the analysis of variance, specially adapted for a two-way classification with unequal numbers (Rao 1952).

Results

The analysis was simplified because there was no significant difference between smokers and non-smokers with regard to age or height (table II).

TABLE II—MEAN FOR AGES AND HEIGHTS OF THE SMOKERS AND NON-SMOKERS

	No.	*Age (yr.)* ± S.E.	*Height (cm.)* ± S.E.
West Finland:			
Smokers	91	35·5 ± 0·86	172·4 ± 0·19
Non-smokers	64	35·6 ± 1·49	173·2 ± 0·25
East Finland:			
Smokers	103	35·5 ± 0·86	169·7 ± 0·22
Non-smokers	39	33·7 ± 1·69	168·5 ± 0·33
Helsinki:			
Smokers	166	38·0 ± 0·66	174·8 ± 0·15
Non-smokers	62	36·4 ± 1·19	174·6 ± 0·24

There was a pronounced relationship between age and serum-cholesterol level in the Finnish samples, as in many other population groups (Keys et al. 1958).

The age trend in serum-cholesterol is shown in table III, which also shows that in each of the three samples the serum-cholesterol level tended to be higher in the smokers than in the non-smokers, the grand average differences being 21, 23, and 23 mg. per 100 ml. in West Finland, East Finland, and Helsinki respectively. In the age-group 50–59 there was no significant difference between smokers and non-smokers in the rural samples, but in Helsinki the difference in serum-cholesterol level reached its maximum.

TABLE III—MEAN TOTAL SERUM-CHOLESTEROL ACCORDING TO AGE

	TOTAL SERUM-CHOLESTEROL (MG. PER 100 ML.)				
Age-groups (yr.)	*20–29*	*30–39*	*40–49*	*50–59*	*Mean* ± S.E.
West Finland:					
Smokers	214	228	244	243	228·7 ± 4·49
Non-smokers	187	203	220	245	208·0 ± 6·15
East Finland:					
Smokers	217	273	261	236	249·7 ± 5·63
Non-smokers	204	245	249	233	226·6 ± 7·74
Helsinki:					
Smokers	219	259	267	290	257·8 ± 3·98
Non-smokers	212	242	244	250	235·1 ± 4·58

When the smoker groups were graded into three subgroups—those smoking (*a*) 10 or fewer, (*b*) 11 to 20, and (*c*) 21 or more cigarettes daily—there was no systematic age trend. The mean cholesterol level rose with the amount smoked; the difference between subgroups (*a*) and (*b*) was 5·1, and between (*a*) and (*c*) 12·7 mg. per 100 ml.

The ratio of men employed in heavy manual work to those in lighter occupations showed no systematic differences either between the non-smokers and smokers, or between the different smoker groups. Thus the differences in the serum-cholesterol level according to the amount smoked are not ascribable to the type of occupation (cf. Keys et al. 1958).

TABLE IV—ARTERIAL BLOOD-PRESSURE ACCORDING TO AGE

	SYSTOLIC BLOOD-PRESSURE (MM. HG)				
Age-groups (yr.)	*20–29*	*30–39*	*40–49*	*50–59*	*Mean* ± S.E.
West Finland:					
Smokers	136	129	135	140	133·2 ± 1·29
Non-smokers	139	135	133	147	139·2 ± 2·12
East Finland:					
Smokers	135	139	132	132	135·4 ± 1·45
Non-smokers	138	149	149	134	142·6 ± 2·46
Helsinki:					
Smokers	120	131	132	136	129·8 ± 0·95
Non-smokers	124	135	138	134	132·8 ± 1·89

	DIASTOLIC BLOOD-PRESSURE (MM. HG)				
Age-groups (yr.)	*20–29*	*30–39*	*40–49*	*50–59*	*Mean* ± S.E.
West Finland:					
Smokers	82	81	83	84	81·9 ± 0·98
Non-smokers	83	84	84	88	84·7 ± 1·35
East Finland:					
Smokers	81	86	85	85	84·1 ± 0·90
Non-smokers	86	88	87	87	86·8 ± 1·51
Helsinki:					
Smokers	82	86	89	91	86·8 ± 0·89
Non-smokers	85	90	92	91	89·6 ± 1·27

The arterial blood-pressure data are summarised in table IV. In all regions and at all ages the blood-pressure tended to be lower among the smokers than among the non-smokers. This was true of systolic, diastolic, and pulse pressures; although the differences were small they are statistically significant.

Table V summarises the skinfold data. Both in West and in East Finland the smokers tended to be thinner than the non-smokers at all ages, except for the 20–29 age-group in West Finland. In Helsinki there was no significant difference between smokers and non-smokers; and these men were, in general, all fatter than the men in the rural samples.

TABLE V—MEAN THICKNESS OF THE SUM OF THE ARM AND SUPRASCAPULAR SKINFOLDS, ACCORDING TO AGE

	ARM AND SUPRASCAPULAR SKINFOLDS (MM.)				
Age-groups (yr.)	*20–29*	*30–39*	*40–49*	*50–59*	*Mean* ± S.E.
West Finland:					
Smokers	17·4	17·8	14·1	14·7	16·7 ± 1·02
Non-smokers	16·6	21·0	19·9	22·9	19·3 ± 1·10
East Finland:					
Smokers	14·4	19·2	17·1	13·1	16·7 ± 0·77
Non-smokers	18·0	21·6	18·8	21·0	19·6 ± 1·24
Helsinki:					
Smokers	27·7	26·8	23·8	28·8	26·1 ± 0·82
Non-smokers	21·7	28·9	27·6	20·6	26·0 ± 1·14

TABLE VI—OVERALL DIFFERENCES BETWEEN REGULAR CIGARETTE SMOKERS (NUMBERING 360) AND NON-SMOKERS (NUMBERING 165)

	Smokers/ non-smokers	*f-test*	P
Age (yr.)	+ 1·09	1·207	..
Total serum-cholesterol (mg. per 100 ml.)	+22·13	30·54	0·001
Systolic blood-pressure (mm. Hg)	− 5·08	14·70	0·001
Diastolic blood-pressure (mm. Hg)	− 2·76	5·67	0·025
Combined skinfold (mm.):			
West and East Finland	− 2·7	6·68	0·025
Helsinki	+ 0·1	..	..

The *f*-values are associated with 1 and 524 degrees of freedom, except for the West + East Finnish sample where the degrees of freedom are 1 and 293. The reference values are approximately $f_{0\cdot001}=11\cdot0$ and $f_{0\cdot025}=5\cdot1$.)

TABLE VII—DIFFERENCES BETWEEN THE SMOKERS OF AMERICAN AND FINNISH-TYPE CIGARETTES IN THE HELSINKI SAMPLE

	Mean		P
	American	*Finnish*	
Age (yr.)	37·0	43·0	..
Total serum-cholesterol (mg. per 100 ml.)	252·0	287·5	0·05 ($f=5\cdot87$)
Systolic blood-pressure (mm. Hg)	129·4	132·0	..
Diastolic blood-pressure (mm. Hg)	86·0	91·0	..

(The *f*-values are associated with 1 and 163 degrees of freedom.)

A statistical summary of the results of the analysis of variance is given in table VI. The most pronounced difference between the smokers and non-smokers is in the serum-cholesterol level, but the difference in systolic blood-pressure is also highly significant. The difference in diastolic blood-pressure is significant but less impressive. No generalisation can be made with regard to relative fatness, though in the rural samples smokers clearly tend to be thinner than non-smokers.

Eventual differences between those smoking American and Finnish cigarettes were also tested. In the rural samples there was no significant difference in the age, serum-cholesterol level, and systolic or diastolic blood-pressure. In the Helsinki sample, the smokers of Finnish cigarettes were older, and other differences were observed (table VII). The differences in blood-pressure could be ascribed to age, but the difference in the serum-cholesterol level was significant at the 0·05 level after the effect of age was eliminated by covariance analysis.

Discussion

It has been reported that heavy smokers in California tend to have higher serum-cholesterol values in the 20–39 age-group but not in the 40–59 age-group (Gofman et al. 1955). But it is not clear whether the smokers and non-smokers were truly comparable in other respects. A statistically significant association between smoking and elevated serum-cholesterol levels was observed in American medical students by Thomas (1958). In the present study it is of interest that in both rural areas the smokers tended to have higher serum-cholesterol values than the non-smokers in each of the three age-groups 20–29, 30–39, and 40–49, but not in the 50–59 age-group. In Helsinki, however, there was a difference between smokers and non-smokers in every age-group, including 50–59; this difference appeared to increase with age, the mean differences in successive decades being 7, 17, 33, and 40 mg. per 100 ml. Among the smokers, those who smoked most tended to have the highest serum-cholesterol level.

Though we have no explanation for these age trends, it does seem that by the time middle age is reached the smokers in Finland generally have had many years of exposure to a higher cholesterol level in the blood than the non-smokers in the same community. This fact should be considered together with the evidence that a higher blood-cholesterol level is associated with an increased susceptibility to ischæmic heart-disease. Here may be, at least in part, an explanation for the reported disparity in heart-disease mortality between smokers and non-smokers.

The difference between the smokers and non-smokers with regard to blood-pressure and fatness does not indicate a greater tendency for smokers to develop heart-disease. But with these variables the differences, though statistically significant, are very small. It is difficult to imagine how an average difference of 5 mm. Hg systolic or of 3 mm. Hg diastolic blood-pressure would influence the development of heart-disease. The same is true of the difference in relative fatness. The measurements of the combined skinfolds indicate that, for the grand average, the non-smokers have a subcutaneous-fat layer that is barely 1 mm. thicker than that of the smokers.

The smoking of Finnish-type cigarettes by some of the men does not explain the differences observed. The blood-pressure values of the two kinds of smokers were identical. There was no difference in serum-cholesterol level in the two rural samples, as against a difference significant at the 0·05 level in the Helsinki sample. This discrepancy may be explained by the Helsinki Finnish-type smokers being a specially self-selected group (only 16% of all smokers).

These data from Finland display interesting differences between smokers and non-smokers. But they do not explain the origin of the differences, and we are not justified in concluding that habitual cigarette smoking *causes* the serum-cholesterol to rise, the blood-pressure to fall, or the body to lose fat. The kind of person who smokes, in contrast to the one who is not inclined to take up smoking, may simply be so constituted otherwise that he tends to have an elevated blood-cholesterol and a low blood-pressure, and to be relatively thin. In a recent 5-year follow-up study we found that men who stop smoking tend to become fatter (Brozek and Keys 1957). This accords with the common observation that smoking depresses the appetite. We cannot explain the reason for the differences in serum-cholesterol and blood-pressure observed in Finland.

Summary

Samples of men aged 20–59 years were studied in rural West Finland, in rural East Finland, and in Helsinki. There were 360 regular cigarette smokers and 165 men who never smoked. At all ages and in all regions, except in the 50–59 age-group in West Finland, the smokers had higher average serum-cholesterol values than the non-smokers. At all ages and in all regions the smokers tended to have slightly lower blood-pressures than the non-smokers. In both rural areas the smokers tended to be slightly thinner than the non-smokers, but in Helsinki there was no clear relation between smoking and body fatness. The relevance of these findings to the reputed high frequency of ischæmic heart-disease among smokers is briefly discussed.

This work was aided by research grants from the Tobacco Industry Research Committee (New York), the Finnish Heart Association (Helsinki), the American Heart Association (New York), the Science Board of the State of Finland, and the Sigrid Juselius Stiftelse (Helsinki).

REFERENCES

Anderson, J. T., Keys, A. (1956) *Clin. Chem.* **2**, 145.
Brozek, J., Keys, A. (1957) *Science*, **129**, 1203.
Committee on Nutritional Anthropometry; chairman A. Keys (1956) *Hum. Biol.* **28**, 111.
Doll, R., Hill, A. B. (1956) *Brit. med. J.* ii, 1071.
Gofman, J. W., Lindgren, F. T., Strisower, B., DeLalla, O. F., Glazier, F., Tamplin, A. (1955) *Geriatrics*, **10**, 349.
Hammond, E. C., Horn, D. (1954) *J. Amer. med. Ass.* **155**, 1316.
— — (1958a) *ibid.* **166**, 1159.
— — (1958b) *ibid.* p. 1294.
Keys, A., Karvonen, M. J., Fidanza, F. (1958) *Lancet*, ii, 175.
Rao, C. R. (1952) Advanced Statistical Methods in Biometric Research; p. 94. New York.
Thomas, C. B. (1958) *J. chron. Dis.* **7**, 198.

TYPE-I POLIOVIRUS ISOLATED FROM A BUDGERIGAR
FURTHER STUDIES

R. G. SOMMERVILLE
M.B. Glasg.*

From the Virus Laboratory, University Departments of Bacteriology and Infectious Diseases, Ruchill Hospital, Glasgow

A STRAIN of type-I poliovirus was isolated recently in this laboratory on three occasions from a budgerigar which was recovering from an acute attack of paralysis of its legs (Sommerville et al. 1958). At the same time an apparently identical virus was found in the stool of a close contact of the bird, a 10-year-old boy in whom fatal bulbar poliomyelitis developed.

The isolation of poliovirus from an avian host was sufficiently unusual to justify further investigation, and the studies reported here were undertaken with three aims. Firstly the properties of the "avian" virus were examined, to see whether it could be differentiated from other poliovirus. Secondly infection of other budgerigars, under laboratory conditions, with the "avian" virus was attempted, in order to observe the course of the infection. Finally the possible association of cage birds kept as household pets with other human cases of paralytic or "non-paralytic" poliomyelitis was investigated.

Properties of the "Avian" Poliovirus

The virus selected for study was isolated from intestinal contents collected from the budgerigar at necropsy. This virus produced characteristic cytopathic changes and multiplied in tissue cultures of the following cells: (*a*) freshly trypsinised rhesus-monkey kidney, human kidney, and human amnion; (*b*) continuous cell lines of human carcinoma strain HeLa, human amnion strain F.L., and monkey kidney strain MK_2. After 2 passages in HeLa and 4 in rhesus-monkey-kidney (R.M.K.) cells a sample of tissue-culture fluid had an infectivity titre (I.D.$_{50}$) of $10^{4\cdot5}$ per 0·1 ml. in R.M.K. cells. No cytopathic changes were produced in cultures of trypsinised kidney from day-old chicks or from young adult budgerigars. Indeed, in cultures of day-old-chick kidney, tubes inoculated with virus degenerated more slowly than control (uninoculated) tubes.

The "avian" virus possessed a titre of $10^{3\cdot5}$ plaque-forming units in R.M.K. cells after 4 passages. Plaques first became visible at 48 hours and had similar size and appearance to those of the stock strain of type-I (Mahoney) poliovirus used as a control. A rabbit antiserum was prepared against the "avian" virus and against type-I (Mahoney) poliovirus by the same method. In each case complete neutralisation was demonstrable when either serum was tested against its homologous or heterologous virus.

The "avian" virus was not pathogenic for suckling or adult mice after inoculation by the intracerebral or intraperitoneal route with or without the simultaneous subcutaneous injection of hydrocortisone.

Infection of Budgerigars and Chickens

BUDGERIGARS

Six young female budgerigars were inoculated in pairs with "avian" virus by various routes. The dose was administered intracerebrally (10^3 I.D.$_{50}$), intraperitoneally ($10^{4\cdot2}$ I.D.$_{50}$) or by polyethylene cannula, into the stomach ($10^{4\cdot2}$ I.D.$_{50}$). Each pair of birds was given virus by two different routes at the beginning of the experiment. The birds were observed daily for 3 weeks; and droppings, collected daily from each cage, were examined for the presence of poliovirus in R.M.K. cells. At the end of the observation period the birds were killed and the brains examined histologically.

Clinical.—No effects were noted until the 14th day after inoculation, when all six inoculated birds suddenly ceased "chattering". Immediately before becoming silent each bird appeared to be drowsy and made curious clicking noises. The onset of the silence was dramatic because the birds had previously been extremely noisy. After several days' silence "chattering" recommenced. During this silent period, "control" uninoculated birds maintained a constant "chatter" in the next room. No paralysis of legs or wings was observed during the 3-week period.

Virological.—Droppings were homogenised to a 10% suspension in Hanks' solution with added antibiotics and freed from bacteria by centrifugation. The pH of the clear supernatant fluid was adjusted to approximately 7 by the addition of sterile sodium bicarbonate, and the extract was examined in R.M.K. cells. No virus was recovered from any bird during any of the 21 days of the experiment. The bowel content collected at necropsy was similarly shown to be free from poliovirus.

Histological.—Examination of the brain tissue revealed no abnormality in the birds which received the virus orally and by the intraperitoneal route. In the four birds which were inoculated intracerebrally no gross lesions were present, but small areas of degeneration were evident among the motor cells. In places these cells were small and sclerosed and surrounded by a group of glial cells. In one brain satellite cells were unusually numerous.

CHICKENS

Twelve 2-day-old chickens were divided into two groups of six. Each group was injected with the same amount of poliovirus by the same combination of routes as the budgerigars. One group of chickens was also injected with 5 mg. hydrocortisone subcutaneously. This injection consisted of equal parts instant and long-acting hydrocortisone. The birds were observed for 21 days, but no paralysis of wings or legs was noted. No "silent period" ensued, and no poliovirus was recovered from the droppings of either group by examination in tissue culture. Histological examinations were not performed on the brains of these birds.

Illness of Budgerigars Related to Poliomyelitis in Home

An attempt was made to assess the frequency of illness in pet budgerigars in relation to poliomyelitis in the home by means of a questionary which was sent to the parents of each child who had been notified as a case of either paralytic or "non-paralytic" poliomyelitis and from whom stool specimens had been examined in this laboratory for virus content during 1956 and 1957. In each case the parent was asked to state: (*a*) whether a cage bird had been kept at the time of onset of the child's illness; (*b*) to classify the bird as budgerigar, canary, or parrot; (*c*) to state whether the bird had been unwell at or about the time of onset of illness in the child; and, if so, (*d*) whether the bird could fly, stand on the perch, or whistle, and whether the bird recovered or died.

Altogether 273 questionaries were sent—108 to homes of children who had sustained a paralytic attack, from

* Sir Maurice Bloch fellow in virology.

most of whom poliovirus had been isolated, and 165 to " non-paralytics " selected to the extent that stool examinations for poliovirus had all been negative. From the two groups 93 and 131 replies respectively were received. The results are summarised in the accompanying table. In 5 and 12 instances respectively a budgerigar became unwell at or about the time of onset of illness in the child; in 3 and 5 instances the bird was unable to

ASSOCIATION BETWEEN ILLNESS IN CAGE BIRDS AND DEVELOPMENT OF PARALYTIC OR " NON-PARALYTIC " POLIOMYELITIS IN CHILDREN IN THE SAME HOUSEHOLD

Type of poliomyelitis	Poliovirus	Total cases	Budgerigar in home	Bird unwell	Unable to			Bird died
					Stand	Fly	" Sing "	
Paralytic	Isolated	60	15	4*	1	1	0	3*
	Not isolated	33	7	2	0	0	1	0
" Non-paralytic "	Not isolated	131	34	12	2	3	0	9

* Includes 1 bat.

stand or to fly, and 2 and 9 birds died; 1 bird was unable to " sing " but recovered, and in 1 home a pet bat became unwell and died shortly before the onset of a paralytic attack of poliomyelitis in the associated child. The numbers involved are too small to draw conclusions, but no significant differences exist between the results obtained from the paralytic and " non-paralytic " groups.

Discussion

From the experimental evidence there is no doubt that the agent originally isolated on three occasions from a single budgerigar was a strain of poliovirus type I; but, in view of our failure to reproduce paralysis in other budgerigars under laboratory conditions with the " avian " virus, the original isolation must be examined critically to ensure, so far as is possible, that no mistake was made.

The original isolation was made in one department of this laboratory, and the finding was sufficiently unusual to warrant a fresh attempt at isolation by another worker on another aliquot of the extract which was prepared from the first specimen of droppings. This second aliquot had been stored frozen in a screw-capped vial and had not been opened between the day of preparation and the second attempt at isolation. Poliovirus type I was isolated readily in HeLa cells. It is extremely unlikely that the HeLa cells were carrying a latent infection with poliovirus, because no other tubes in the batch degenerated spontaneously, and, although the remainder were used for isolation purposes, no other polioviruses were grown. The third and fourth isolations were made two weeks later, after the infected bird had been delivered to the animal house, situated close to the laboratory. Shortly after the bird was delivered, a fresh specimen of droppings collected from the cage was examined in HeLa cells. On the same afternoon the bird was killed and at necropsy the bowel was removed, opened in the laboratory, and the contents collected, extracted, and examined in HeLa cells. From each specimen poliovirus type I was isolated readily, and again contamination of the HeLa cells by latent poliovirus could be excluded.

The common factor between the first, second, and third isolation was the person who prepared the extracts from the droppings. 2 weeks elapsed between the preparation of the first extract, which yielded poliovirus type I on two occasions, and the second extract from droppings collected immediately before the bird was killed. The extract of the bowel content collected at necropsy was prepared by a different individual working in a laboratory in which cultures of poliovirus had not been stored or maintained for at least two years.

If accidental contamination is to be considered as a possible explanation of the findings, a strange twist of fate must have been responsible for the accidental introduction of three type-I poliovirus strains into three separately prepared extracts of " droppings ". Accidental transmission by latent infection of HeLa cells can, moreover, be excluded because spontaneously degenerating HeLa cells have not been encountered in this laboratory (other than those obviously accounted for by bacterial contamination) and because of the absence of poliovirus isolations from other tubes of the same batch under examination at the same time.

In view of the findings reported here, I believe that the original isolations of virus were actually made from the budgerigar. The significance of the poliovirus for the budgerigar is questionable, however, in view of the experimental evidence reported here and the observations by Dick and Dane (1958) and Dane et al. (1959) who were unable to reproduce paralysis or to cause an antibody response in budgerigars inoculated with several strains of poliovirus. Similarly Dekking (1958) was unable to demonstrate poliovirus antibody in avian sera. The presence of some unidentified toxin, metabolic disturbance, bacterium, or indeed virus (Markson 1958) may have been responsible for the paralysis, and the poliovirus could then have been of secondary importance in the bird's condition. Under the circumstances, the ability of the bird to maintain poliovirus type I within its alimentary tract conditioned by some other disease process is of considerable interest.

Summary

The characters of a strain of poliovirus type I originally isolated from a budgerigar recovering from an attack of paralysis involving the legs have been examined.

Attempts to infect further budgerigars with the virus were unsuccessful, although all the birds became unwell between the 15th and 21st days following inoculation. No effect was observed in chickens after inoculation of the virus with or without the simultaneous administration of hydrocortisone.

A postal survey of 224 families in which there had been a known case of poliomyelitis revealed that 56 maintained budgerigars as a family pet, and that in 17 instances the birds died at about the same time as a child in the house contracted paralytic or " non-paralytic " poliomyelitis. Illness in the budgerigar could not be correlated with the laboratory demonstration of poliovirus in the child's stool.

I should like to thank Dr. G. B. S. Roberts, pathologist, Ruchill Hospital, for the histological examinations; Mrs. E. G. Diamond and Miss E. G. S. McIntosh, B.SC., for assistance with the postal survey; Dr. R. B. Morrison, Glasgow University, for the F.L. strain of human amnion cells; and Dr. N. S. Mair, Public Health Laboratory, Leicester, for the MK_2 line of monkey-kidney cells.

REFERENCES

Dane, D. S., Dick, G. W. A., Donaldson, S. N., Briggs, M., Nelson, R. (1959) *Lancet*, i, p. 497.
Dekking, F. (1958) *ibid.* i, 799.
Dick, G. W. A., Dane, D. S. (1958) *ibid.* p. 585.
Markson, L. M. (1958) *ibid.* p. 689.
Sommerville, R. G., Monro, I. C., Cuthbert, C. C. (1958) *ibid.* p. 512.

BUDGERIGARS AND POLIOMYELITIS

D. S. DANE
B.A., M.B. Cantab.
LECTURER IN MICROBIOLOGY, QUEEN'S UNIVERSITY, BELFAST

G. W. A. DICK
M.D., D.Sc. Edin., F.R.C.P.E.
PROFESSOR OF MICROBIOLOGY, QUEEN'S UNIVERSITY, BELFAST

S. N. DONALDSON
M.B. Belf., D.P.H.
ASSISTANT MEDICAL OFFICER OF HEALTH, BELFAST

With the assistance of
MOYA BRIGGS, B.Sc. Belf., and R. NELSON

RECENTLY Sommerville et al. (1958) reported the isolation of type-I poliovirus from the fæces of a sick budgerigar in a household where a child died of an acute type-I poliovirus infection. Though we were unable on a previous occasion to infect budgerigars with a virulent strain of type-I poliovirus (Dick and Dane 1958), and though neither we nor Dekking (1958) could find poliovirus neutralising antibody in the blood of normal budgerigars, we considered the problem deserved further investigation.

In this paper we describe unsuccessful attempts to infect budgerigars with eleven different poliovirus strains from various sources, and give the results of a small epidemiological inquiry.

Materials and Methods

Tissue cultures.—Monkey-kidney monolayer tissue cultures were used for the isolation of viruses and for virus-neutralisation tests. Details of these techniques have been described previously (Dane et al. 1956).

Virus isolation.—Fæcal and organ suspensions were tested to detect virus at levels of $10^{1\cdot7}$ T.C.D.$_{50}$ per g. and then titrated if positive.

Virus-neutralisation tests.—Budgerigar sera were screened for poliovirus antibody at a 1 in 10 dilution against 100 T.C.D.$_{50}$ of virus.

Budgerigars.—A heterogeneous collection of adult birds was assembled from a variety of sources for the experiments, which were conducted during the months of March, April, and May. Blood specimens were taken from the wing vein; the amount collected at any one time was about 0·5 ml.

Intracerebral inoculation.—0·06 ml. of virus suspension was inoculated into the brain.

Oral inoculation.—0·2 ml. of virus suspension was injected into the œsophagus using a syringe fitted with polyethylene tubing.

Experimental

The origin and history of the eleven different strains of poliovirus used in the experiments are summarised in the accompanying table. Each strain of virus was fed to three birds which were kept in the same cage. Fresh fæcal specimens were collected daily for the first week and then on every second or third day until the twenty-sixth day. On the thirtieth day after virus feeding the birds were inoculated intracerebrally with the same virus with which they had been fed, and they were then observed for a further period of thirty days. Blood samples were taken from each bird, before virus was fed, at the time of intracerebral inoculation, and one month later.

No virus was found in the fæces of any of the birds except those of group "O", whose pooled fæces had titres of $10^{3\cdot8}$ T.C.D.$_{50}$ and $10^{2\cdot3}$ T.C.D.$_{50}$ respectively per g. of fæces on the first and second day after feeding but at no other time.

No bird had any demonstrable neutralising antibody to any of the three types of poliovirus at the start of the experiment. At the conclusion of the experiment, one month after intracerebral inoculation, birds nos. 14 and 15 from group "O" were found to have developed low titre (1:10) neutralising antibody to type-I poliovirus. None of the other birds had developed detectable antibody to the type of poliovirus fed and inoculated.

During the progress of the experiment seven birds (nos. 13, 17, 21, 24, 30, 34, and 55) died from unknown causes. The comparatively large amounts of blood which were collected from the birds may have accounted for at least some of these deaths. At no time was any paralysis observed in any bird. Suspensions of brain and gut (with contents) of birds which died were inoculated into tissue cultures. Type-I poliovirus was found in the brain of bird no. 30 at a titre of $10^{2\cdot6}$ T.C.D.$_{50}$ per g. when it died two days after intracerebral inoculation with $10^{3\cdot9}$ T.C.D.$_{50}$ of this virus. No virus was isolated from any of the remaining six birds which died.

Other Investigations

Local breeders of budgerigars were asked to send any paralysed birds which they owned to this laboratory for investigation. In all, we received five "paralysed" birds.

On examination each of these birds was found to have one deformed or weak leg, and in four cases the deformity appeared to have been due to a past bone fracture. In the remaining bird a large renal tumour was found extending over the sciatic nerve on the same side as the weak leg, which in this case showed no evidence of a previous fracture. Blood samples taken from these five birds showed no neutralising antibody to any of the three types of poliovirus.

The total number of budgerigars which we have examined serologically for evidence of past poliovirus infection is now fifty, and all the tests have been negative.

In Belfast, during 1957, there were nearly two hundred cases of acute poliomyelitis and aseptic meningitis. The large majority of these illnesses were caused by type-I poliovirus and occurred in children under 6 years of age. In a follow-up inquiry into the state of health of patients some months after their discharge from hospital, ninety-nine families with poliomyelitis infections were questioned about their pet animals and birds. If they kept or had kept budgerigars they were asked about the past health of these pets. Seventy-three of the patients involved in

DATA ON 11 STRAINS OF POLIOVIRUS USED IN EXPERIMENTS

Group	Serial nos. of birds	Poliovirus type used	Log$_{10}$ T.C.D.$_{50}$ of virus suspension used	Origin of virus strain	Passage history *
H	22, 38, 39	I	6·6	Fæces of paralytic case	1st pass
B	21, 25, 27	I	7·2	Fæces of normal child	1st pass
N	33, 34, 35	III	5·6	Fæces of non-paralytic case	2nd pass
O	14, 15, 50	I	8·1	Mahoney laboratory strain †	Numerous passages
M	24, 40, 42	III	4·3	Fæces of non-paralytic case	2nd pass
R	28, 29, 52	I	6·3	Fæces of bulbar case	1st pass
S	45, 49, 51	I	5·8	Fæces of fatal case	1st pass
P	30, 31, 32	I	5·1	Fæces of paralytic case	20% fæcal suspension
U	53, 54, 56	I	4·8	SM, N 90 vaccine virus ‡	Numerous passages
Q	13, 16, 17	I	3·3	Fæces of paralytic case	20% fæcal suspension
T	46, 48, 55	II	4·6	Fæces of paralytic case	2nd pass

* All virus passages in this laboratory were made in monkey-kidney tissue cultures.
† Drom Dr. W. Wood, Glaxo Laboratories.
‡ From Lederle Laboratories.

this inquiry had been paralysed, and twenty-six had suffered from aseptic meningitis. In every case type-1 poliovirus had been isolated from fæcal specimens during the patient's illness. Of the seventy-three paralysed patients, twenty-four kept pet budgerigars. Two deaths had occurred amongst their birds—in one case two months before the patient's admission to hospital and in the other two weeks after. Of the twenty-six patients who had had non-paralytic poliomyelitis, six kept budgerigars and in two instances birds had died. In the first case two budgerigars died about the same time as the child became ill, and in the second case a budgerigar died the day after the child entered hospital. This second case was interesting because the small boy who became ill was allowed by his parents to "kiss" his pet, but his two siblings were not. It should be noted, however, that the boy was in contact a fortnight before his illness with a relative who one week after their meeting developed paralytic poliomyelitis (type-1 poliovirus).

Discussion

Our interpretation of the experimental results reported above is that we failed to infect any of the budgerigars with any of the poliovirus strains which were fed or inoculated. We do not consider that the development of low-titre antibody by two birds is evidence that they were infected with poliovirus. Connolly and Dick (1958) have shown that children may develop antibody after inactivated poliovirus has been given by mouth, and these two birds had been fed a large dose of virus ($10^{7\cdot4}$ T.C.D.$_{50}$). Likewise the recovery of small amounts of virus from the pooled fæces of birds nos. 14, 15, and 50 on the first two days after feeding is not considered as evidence of gut infection, but as purely passive excretion. Virus was recovered from only one of seven birds which died during the experiment, and then only in the brain in smaller amounts than the bird had received intracerebrally two days earlier. Thus we have no evidence that any of the seven birds died from a poliovirus infection.

The absence of poliovirus neutralising antibody in the blood of the fifty budgerigars examined, together with our unsuccessful attempt to find birds with residual paralysis which might have been caused by a past poliovirus infection is strong evidence that budgerigars do not often become infected with, or paralysed by, polioviruses, and that they are unlikely to be of importance in the spread of the disease. This does not rule out the possibility that budgerigars may occasionally become infected by people excreting poliovirus and then later transmit the virus to other human contacts. The results of the inquiry into the health of pet budgerigars owned by patients who had suffered from poliomyelitis was surprising. Three of thirty patients who kept budgerigars reported the death of at least one bird within two weeks of the onset of their illness. We do not think that any attempt to evaluate the significance of this is likely to give a clear answer. However, it is sufficiently suggestive to encourage us to continue the search for associations between human poliomyelitis and poliovirus infection in budgerigars. Unless others can succeed in infecting budgerigars experimentally, confirmation of the report by Sommerville et al. (1958) may have to await a similar recovery of virus from a naturally infected bird.

Summary

Budgerigars proved resistant to infection with eleven different strains of poliovirus given by the oral and intracerebral routes.

No evidence could be found that budgerigars are at all commonly infected with polioviruses in Northern Ireland.

Thirty out of ninety-nine poliomyelitis patients questioned kept pet budgerigars. Three of the thirty reported the death of one or two birds about the time of their illness.

We would like to thank local budgerigar breeders for their cooperation, and Mr. F. Burns, F.I.M.L.T., for his help.

REFERENCES

Connolly, J. H., Dick, G. W. A. (1958) *Lancet*, ii, 333.
Dane, D. S., Dick, G. W. A., Connolly, J. H., Briggs, E. M., McLeod, W.J. (1956) *ibid.* i, 481.
Dekking, F. (1958) *ibid.* i, 799.
Dick, G. W. A., Dane, D. S. (1958) *ibid.* p. 585.
Sommerville, R. G., Monro, I. C., Cuthbert, C. C. (1958) *ibid.* p. 512.

URINARY 17-KETOSTEROIDS AND KETOGENIC STEROIDS IN A MIXED JAMAICAN POPULATION

G. F. BLANE
B.Sc., Ph.D. Southampton
LECTURER IN PHARMACOLOGY,
UNIVERSITY COLLEGE OF THE WEST INDIES, JAMAICA

THE suggestion has been made that adrenal activity may be low in coloured races. Thus, Barnicot and Wolffson (1952) reported a mean 24-hour urinary 17-ketosteroid (17-K.S.) value of 7·97 mg. for 37 West Africans. 27 Europeans living in Africa under the same conditions gave a mean value of 13·71 mg. per day. Friedmann (1954) compared the 17-K.S. output of North and South Indians with expatriate Europeans. While there was no significant difference between the South Indians (mean value 10·81 mg.) and the lighter North Indians (10·00 mg.), the very significantly higher mean of 21·28 mg. per day was obtained from the Europeans. Material for both these studies was obtained from healthy men, mostly in their third decade.

Stirling and Keating (1958) have reported the finding of adrenal weights which were very low by European standards in glands taken post mortem from 107 Jamaicans of mixed African descent. They found, furthermore, that the low weights were due to the small size of the cortex, and that the medullary weight was more or less "normal".

The present report is concerned with preliminary observations on the urinary excretion of 17-K.S., and also 17-ketogenic steroids (17-K.G.S.) by coloured Jamaicans and Europeans living in Jamaica.

Material and Methods

Samples were collected only from men aged 19–27. All were in good health and receiving an adequate and balanced diet. The Jamaican samples were supplied mostly by medical students; a few samples came from a Jamaican army unit. The Europeans were either members of the junior staff of the University College of the West Indies or soldiers serving with a British regiment in Jamaica. Most of the Europeans had not been in the tropics more than a year. Every effort was made to eliminate unnecessary stresses on, and immediately before, the day of urine collection.

Urines were made up to 1500 ml. on the morning of delivery and stored without the addition of preservative at +5°C. Normally they were analysed within 3 days of collection.

17-K.G.S. were determined by a modification of the method of Gibson and Norymberski (1954), but using benzene for the extraction stage instead of ethylene dichloride, as recommended by Jorgensen (1957). The 17-K. extracts were prepared by a method slightly modified from that of

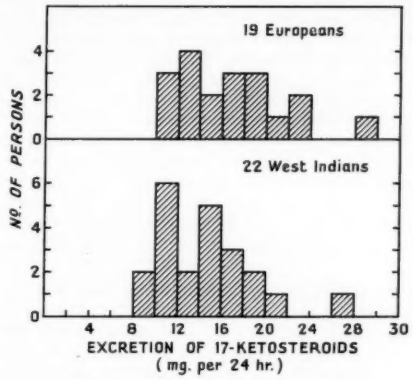


Fig. 1—Urinary excretion of 17-K.S.

Drekter et al. (1952) involving the use of sodium-hydroxide pellets instead of an aqueous solution at the "alkaline wash" stage. Colorimetry was by the Pearson and Giaccone (1948) modification of the Zimmermann reaction, using dehydroisoandrosterone as the standard steroid. The colours were read at 520 mμ in a Beckmann DU spectrophotometer.

Several urines were assayed concurrently by the original method of Norymberski et al. (1953), and by that of Gibson and Norymberski (1954). The results so obtained did not differ significantly from those obtained by my modification.

Results

In 19 Europeans values obtained ranged between 10·4 mg. and 28·5 mg. per 24 hours for 17-K.S. output and between 6·7 mg. and 14·1 mg. per 24 hours for 17-K.G.S. output. The mean values (±S.E.) were 16·68±1·116 mg. and 9·63±0·428 mg. respectively.

The range in 22 West Indians was from 8·9 mg. to 27·5 mg. per 24 hours for 17-K.S., and from 2·7 mg. to 10·6 mg. per 24 hours for 17-K.G.S. The means for this group were 14·72 mg. ± 0·948 mg. and 6·50 ± 0·503 mg. respectively.

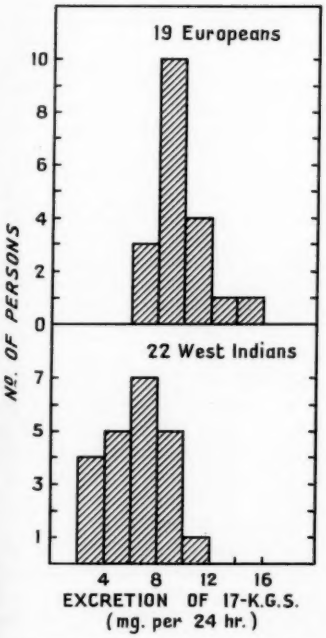


Fig. 2—Urinary excretion of 17-K.G.S.

Among the West Indians, who varied in colour from very light brown to black, there was no evidence whatever of correlation between degree of pigmentation and excretion of either steroid fraction. For the purposes of analysis, therefore, it is possible to treat the West Indians only as a "mixed coloured population".

Figs. 1 and 2 illustrate the range of values for both assays. The similarity in distribution pattern of 17-K.S. output of Europeans and West Indians is evident from fig. 1. Analysis showed no significant difference between the two sets of 17-K.S. values ($P = <0·2, >0·1$).

By contrast, the 17-K.G.S. values for West Indians are clearly grouped more towards the lower end of the scale than are those for the Europeans (fig. 2). Student's "t" test here showed a highly significant difference between the means ($P = <0·001$).

Discussion

Earlier workers have put forward several hypotheses on the relationship between adrenal cortical activity and ethnic skin pigmentation, citing apparent racial differences in 17-K.S. output as their main evidence. At all times simple 17-K.S. values should be treated with great caution —primarily because, particularly when comparing groups of men, the percentile contribution from the products of testosterone catabolism is ill-defined. Due consideration must also be given to the known relationship between 17-K.S. output and diet (Landau et al. 1948, Kinsell et al. 1952) as well as the possibility of modified metabolic pathways in the steroid catabolism of different races.

The results of the present, admittedly limited, study detract from the thesis that the degree of ethnic pigmentation is inversely related to cortical activity, at least as estimated by 17-K.S. determinations.

The urinary 17-K.G.S., on the other hand, are generally considered to provide one of the best indices of adrenal cortical activity available to us today (Borth 1956, Sobel et al. 1958), representing the physiologically important 17-hydroxylated "glucocorticoids". By contrast with the essentially "normal" 17-K.S. values obtained from West Indian subjects, the 17-K.G.S. values were generally low. Of 22 normal healthy individuals 9 excreted less than 6 mg. 17-K.G.S. per 24 hours on the test day. These values would appear to be considerably lower than the lowest normally recorded for men of European stock and might therefore be considered suggestive of adrenal insufficiency in the Jamaicans.

Two alternative hypotheses may be tentatively advanced:

1. It would seem possible that the corticoid output of coloured West Indians is in fact low, in which case the 17-K.G.S. values obtained truly represent the state of adrenal activity. Such a thesis is compatible with the finding of low adrenal weights (Stirling and Keating 1958). Should this be the case it would appear that the requirement for corticoids may be less among West Indians than among Caucasians.

2. Alternatively there may be minor differences in the metabolic disposal of corticoids in different populations. In this case the West Indian 17-K.G.S. values might misrepresent the state of cortical activity when compared with data from other populations.

An investigation of circulating hydroxycorticoid levels in Europeans and Jamaicans is in course of preparation; and this may enable more definite conclusions to be reached.

Finally, the 17-K.G.S. values for the Europeans themselves tended to be rather low by accepted standards. It is proposed to investigate further the changes in steroid-excretion patterns of Europeans after taking up residence in the tropics.

Summary

The mean daily 17-ketosteroid excretion for a group of coloured Jamaicans was not found to be significantly different from that of Europeans living under the same conditions.

Mean 17-ketogenic steroid excretion was significantly lower in the Jamaicans.

References overleaf

NEPHROTIC SYNDROME WITH POLLEN HYPERSENSITIVITY

J. HARDWICKE
M.D. Birm., B.Sc. Lond.

J. F. SOOTHILL
M.A., M.B. Cantab., M.R.C.P.

J. R. SQUIRE
M.D. Cantab., F.R.C.P.

G. HOLTI
M.D. Leeds

From the Department of Experimental Pathology, University of Birmingham, and the Medical Research Council Unit for Research on the Experimental Pathology of the Skin

IT is now recognised that proteinuria of sufficient severity will lead to the development of a nephrotic syndrome. In recent years many authors have called attention to the diversity of conditions which may produce such proteinuria, though the anatomical lesion of the kidney causing leakage of plasma-proteins remains uncertain (Kark et al. 1958, Squire, Blainey, and Hardwicke 1957). A few cases of massive proteinuria and nephrotic syndrome reported previously have been either associated with skin hypersensitivity (Fanconi et al. 1951) or causally related to a specific sensitising agent, such as poison-ivy (Rytand 1948), or a bee-sting (Rytand 1955); these patients were mostly children. We report the case of an adult male in whom attacks of proteinuria and the nephrotic syndrome were apparently associated with sensitivity to pollen; an unusual and perhaps specific histological change was demonstrated in the kidney on biopsy.

Case-report

The patient is a schoolmaster aged 45. Between 1949 and 1955, he had six fully developed attacks of nephrotic syndrome, all starting between July and September, and all except one resolving spontaneously in 3-6 weeks. The urine was not tested in every attack, but proteinuria was found in most; frothing of the urine was noted during each attack, and was absent during remission.

He first came to us (during the seventh episode) in October, 1955, with a massive proteinuria and pitting œdema of the lower limbs, extending up to the mid-thighs. There was a moderate degree of muscular wasting. He looked unwell and complained of feeling tired. Despite the repeated renal disorder the blood-pressure was 115/80 mm Hg. Apart from a moderate degree of ascites, no other abnormality was found on physical examination.

Investigation confirmed a nephrotic syndrome (fig. 1): proteinuria 10 g. per day, serum-albumin 1·8 g. per 100 ml., and other serum-protein changes typical of nephrotic syndrome; serum-cholesterol 1050 mg. per 100 ml. and serum-complement 1.22 units. Creatinine-clearance 70 ml. per min. and blood-urea 25 mg. per 100 ml. The urine contained no deposit.

MR BLANE : REFERENCES

Barnicot, N. A., Wolffson, D. (1952) *Lancet*, i, 893.
Borth, R. (1956) *Acta endocr., Copenhagen*, **22**, 125.
Drekter, I. J., Heisler, A., Scism, G. R., Stern, S., Pearson, S., McGavack, T. (1952) *J. clin. Endocrin.* **12**, 55.
Friedmann, H. C. (1954) *Lancet*, ii, 262.
Gibson, G., Norymberski, J. K. (1954) *Ann. rheum. Dis.* **13**, 59.
Jorgensen, M. (1957) *Acta endocr., Copenhagen*, **26**, 424.
Kinsell, L. W., Partridge, J. W., Boling, L., Margen, S. (1952) *Ann. intern. Med.* **37**, 921.
Landau, R. L., Knowlton, K., Anderson, D., Brandt, M. B., Kenyon, A. T. (1948) *J. clin. Endocrin.* **8**, 133.
Norymberski, J. K., Stubbs, R. D., West, H. F. (1953) *Lancet*, i, 1276.
Pearson, S., Giaccone, S. (1948) *J. clin. Endocrin.* **8**, 618.
Sobel, C., Golub, O. J., Henry, R. J., Jacobs, S. L., Basu, G. K. (1958) *ibid.* **18**, 208.
Stirling, G. A., Keating, V. (1958) *Brit. med. J.* ii, 1016.

He refused admission to hospital until after the school term finished, and a short course of cortisone was ineffective. On admission in December his condition was unchanged. The total white-cell count was normal; but direct counting revealed an eosinophilia of 1100 per c.mm., though later the eosinophil-count has always been normal. Skin tests showed a definite sensitivity to tree and grass pollens, and on questioning he admitted to mild hayfever, which was worse while taking schoolboys haymaking during the summer vacations. Treatment with cortisone 75 mg. per day was started, and within 10 days the proteinuria disappeared; this was followed by rapid remission of the nephrotic syndrome (fig. 1).

He was discharged from hospital in January. Cortisone was continued throughout 1956, though the dose was reduced to 50 mg. daily in April. In July a trace of protein was found in the urine, but he remained well until September, when, after a holiday in the country, he again developed œdema and proteinuria.

He was readmitted in October, 1956, with a proteinuria of 10-12 g. per day and with the changes of nephrotic syndrome in the serum-proteins (fig. 1). This time the creatinine-clearance showed a sharp fall from 80–120 ml. per min. to 20–25. Skin-testing showed a very greatly increased sensitivity to the same allergens as before (fig. 1). The dose of cortisone was increased to 100 mg. per day, and again the response was rapid; within a month protein was absent from the urine. The creatinine-clearance also rapidly returned to the previous levels, and an intravenous pyelogram showed no abnormality.

A percutaneous biopsy of the kidney, taken by the method of Kark and Muehrcke (1954), shows :

Adequate cortex and medulla are present.

All the glomeruli, apart from two hyalinised ones, appear normal. The tubules are dilated, with hyaline-droplet change and amorphous debris in the lumen. In one area there is tubular atrophy, with fibrosis and thickening of the basement membrane.

In two areas of the interstitial tissue, one juxtaglomerular, and the other between tubules in the cortex, there are zones of cellular infiltration with small round-cells, plasma-cells, and a striking excess of eosinophils. Eosinophils are also seen between the tubules in the medulla (fig. 2).

Since discharge in November, the patient has had cortisone; the initial dose of 100 mg. daily was later reduced gradually to 50 mg. daily. Clinically his condition has remained normal, and renal-function tests reveal no abnormality. The urine has been protein-free, and the deposit has never contained an excess of red or white blood-cells, though hyaline casts were present where there was proteinuria. Unfortunately the deposit was not examined for eosinophils.

Courses of desensitising injections with mixed-pollen vaccine (Bencard) have been given over the last 2 years, and skin tests since April, 1958, have shown much less sensitivity (fig. 1).

The patient has now had, under cover of cortisone, his first 2 years in 7 free from an attack of proteinuria and nephrotic syndrome. The cortisone is now being withdrawn, and he will be watched carefully for any relapse.

Discussion

While there seem to be strong grounds for postulating an allergic basis in this case, evidence of such an ætiology is in our experience extremely rare. This is the only case in a series of more than eighty nephrotics examined in this department during a period of more than 6 years. A history of seven attacks of the nephrotic syndrome in 7 years with a seasonal incidence is unusual.

In this case despite the recurrent attacks, no evidence of residual renal damage was shown by the creatinine-clearance test; although clearance was severely reduced during relapse, it returned rapidly to normal after remission.

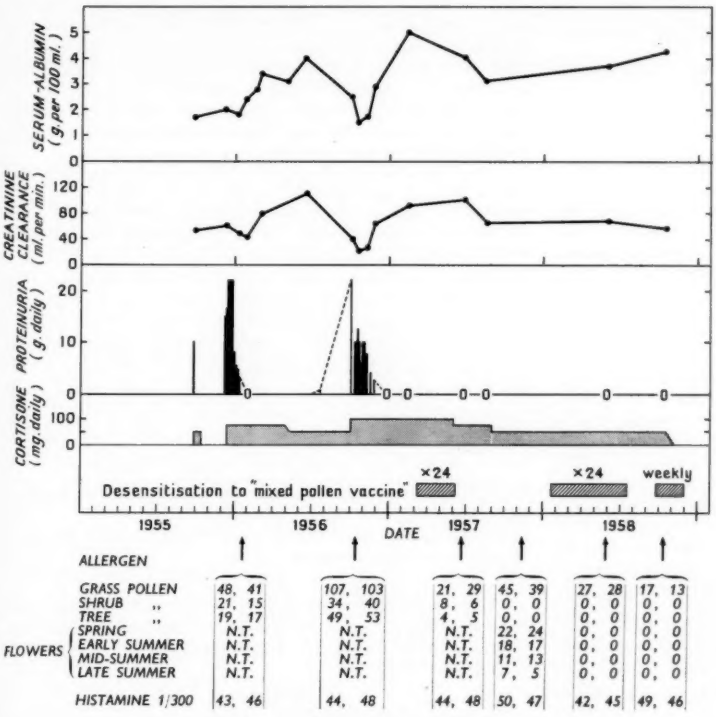

SERUM-ALBUMIN (g. per 100 ml.)
CREATININE CLEARANCE (ml. per min.)
PROTEINURIA (g. daily)
CORTISONE (mg. daily)
Desensitisation to "mixed pollen vaccine"
×24
×24
weekly
1955
1956
1957
1958
DATE
ALLERGEN
GRASS POLLEN 48, 41 107, 103 21, 29 45, 39 27, 28 17, 13
SHRUB ,, 21, 15 34, 40 8, 6 0, 0 0, 0 0, 0
TREE ,, 19, 17 49, 53 4, 5 0, 0 0, 0 0, 0
FLOWERS SPRING N.T. N.T. N.T. 22, 24 0, 0 0, 0
EARLY SUMMER N.T. N.T. N.T. 18, 17 0, 0 0, 0
MID-SUMMER N.T. N.T. N.T. 11, 13 0, 0 0, 0
LATE SUMMER N.T. N.T. N.T. 7, 5 0, 0 0, 0
HISTAMINE 1/300 43, 46 44, 48 44, 48 50, 47 42, 45 49, 46

Fig. 1—Clinical progress of the patient.

Figures in columns are duplicate measurements of mean diameters (mm.) of wheals to the respective allergens on the dates indicated by the arrows.

The first and third courses of desensitising injections were against grass, shrub, and tree pollens only; to the second course mixed flower pollens were added.

N.T. = not tested.

That the attacks were related to the patient's hypersensitivity to pollens is suggested by the dramatic increase in the response to the skin tests during the period of relapse. Fanconi et al. (1951) found hypersensitivity of the skin in some nephrotic children, but were unable to correlate increases in sensitivity with aggravation of the renal disease. We have subjected nineteen patients with the nephrotic syndrome to routine skin-testing; apart from this case, two others showed reactions to tree and shrub pollens. One of these, a young man of 18, has periorbital eczema which becomes worse during periods of increased proteinuria. The other, a woman of 44, has no allergic symptoms.

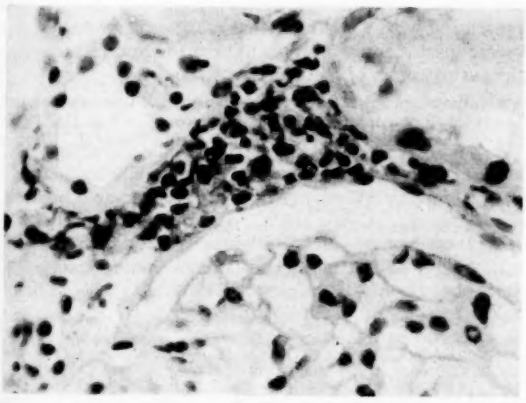


Fig. 2—Area of cellular infiltration seen microscopically in the biopsy specimen of kidney. Most cells in this area are eosinophil leucocytes. The edge of a normal glomerulus is also seen. (Hæmatoxylin and eosin. × 600.)

Although a high eosinophil-count was found at first in the case now reported, the circulating eosinophils did not rise again during relapse when he was taking cortisone. In spite of this, focal infiltration with eosinophils was demonstrated at that time on renal biopsy; the infiltration was seen in both cortex and medulla but only in the interstitial tissues, and it was not apparently related to vessels, or to any particular part of the nephron. Eosinophilia has been recorded previously in the nephrotic syndrome (McCall 1952) particularly in children. In our predominantly adult series only two other patients, one of them the young man of 18, and the other a boy of 7, had a significant eosinophilia.

Nineteen of our patients with nephrotic syndrome have shown a satisfactory response to cortisone. Of these, six have had temporary relapses while on cortisone in the following months: January (1), June (1), August (2), September (1), and November (1). Although there was a substantial reduction in proteinuria in all of them, the urine became free of protein in only seven. In four this occurred within 3 months; in the other three it took more than a year.

Our present case showed an unusually rapid response to cortisone for an adult. His urine became protein-free in the first occasion within 10 days of starting treatment with 75 mg. per day, and on the second occasion within 2 months of increasing the dose to 100 mg. per day. In this respect his response to cortisone resembles more closely that of children than that of adults with this syndrome (Metcoff 1956). It seems probable that the variation in response is related to the ætiology of the renal disease, but there is no evidence to suggest that most cases of nephrotic syndrome in children are similar in ætiology to this adult case. It would also be unwise to suggest that there was a direct causal relationship between allergy and the nephrotic syndrome in a substantial proportion of cases; if this were so then the condition should be encountered frequently in allergy clinics. The striking correlation in this case, however, suggests that skin tests to possible allergens should be made in cases of heavy proteinuria.

Summary

A patient with recurrent attacks of the nephrotic syndrome is described. The history strongly suggested an allergic basis, and this was supported by the results of skin-testing and by the finding of eosinophilic infiltration in a biopsy of the kidney.

Rapid remission was induced by cortisone therapy. A trial of desensitisation to tree and grass pollens has been undertaken.

We are particularly indebted to Prof. R. M. Kark, who called our attention to the eosinophilic infiltration in this case, and to Dr. D. B. Brewer for help with the histology.

REFERENCES

Fanconi, G., Kowmine, C., Frischknecht, W. (1951) *Helv. Pædiat. acta.* **6,** 199.
Kark, R. M., Muehrcke, R. C. (1954) *Lancet*, **i,** 1047.
— Pirani, C. L., Pollak, V. E., Muehrcke, R. C., Blainey, J. D. (1958) *Ann. intern. Med.* **49,** 751.
McCall, M. F. (1952) *Arch. Dis. Childh.* **27,** 309.
Metcoff, J. (1956) Proceedings of the 8th Annual Conference on Nephrotic Syndrome; p. 158.
Rytand, D. A. (1948) *Amer. J. Med.* **5,** 548.
— (1955) *Stanf. med. Bull.* **13,** 224.
Squire, J. R., Blainey, J. D., Hardwicke, J. (1957) *Brit. med. Bull.* **13,** 43.

PLATELET DYSFUNCTION

A. K. FRAZER
M.A. Cantab., M.B. Lpool
LATE REGISTRAR, DEPARTMENT OF PATHOLOGY, WOMEN'S HOSPITAL, LIVERPOOL

WHILST thrombocytopenic purpura is not a rare cause of dysfunctional uterine hæmorrhage (Buxton 1941, Dameshek and Rheingold 1949), thromboasthenia, in which there is a disturbance not of platelet numbers but of platelet function, is extremely uncommon (Biggs and Macfarlane 1957). In thrombocytopenic purpura the defect is in the formation of the platelet-thromboplastic factor (de Nicola 1954, Bonnin 1956); therefore the cause of the symptoms may be a dysfunction rather than a shortage of platelets. In thromboasthenia, although the platelet-count remains within the normal range, the ability to produce platelet-thromboplastic factor is grossly deficient (Braunsteiner 1955); therefore purpuric bleeding occurs.

The following case of dysfunctional uterine hæmorrhage may be classified in the group of hæmorrhagic diatheses due to platelet dysfunction.

Case-report

A woman, aged 40, had been married 5 years and had had two children, the last 3 years previously. Menarche was at 14 and the menstrual cycle was usually 7/28 but since her last confinement had been 14/21.

3 months before admission to hospital on Feb. 23, 1957, she had had uterine bleeding almost continuously for 7 weeks followed by irregular losses. She gave a history of bruising easily, often without obvious trauma. There was no family history of excessive bleeding; but her mother had had a hysterectomy for uterine hæmorrhage at the age of 30. On examination all systems appeared normal; there was no gross gynæcological lesion.

A symptomatic diagnosis of epimenorrhagia was made.

Laboratory findings

Hæmoglobin 9·5 g. per 100 ml. (65%); packed-cell volume 30%. A blood-film showed that the red cells were hypochromic, but the white cells appeared normal; the platelets were plentiful but there were some abnormally large forms. The platelet-count varied between 180,000 per c.mm. and 240,000. The tourniquet test was positive. The bleeding-time (Ivy et al. 1940) was within normal limits on the first occasion ($4^1/_2$ minutes) and increased on two other occasions (8 minutes and 13 minutes).

The whole-blood coagulation-time was 26 minutes, using the Lee and White (1913) method with silicone-treated test-tubes (normal range in this laboratory 18–30 minutes). The prothrombin-time (Quick 1935) was 12 seconds—i.e., 100% prothrombin activity. The result of the prothrombin-consumption test, which was equivocal, was 20 seconds; a one-stage technique was used (Quick 1951). This test was repeated several times with the same result. Clot-retraction (Ackroyd 1949) was 56·5%; there was no lysis of the clot at 37°C within 24 hours. The plasma-fibrinogen level was 183 mg. per 100 ml.

The bone-marrow showed a simple myeloerythroid hyperplasia. The megakaryocytes were not increased in number, and had no abnormal features.

The thromboplastin-generation test (Biggs and Douglas 1953), using a suspension of 1,000,000 platelets per c. mm., showed that the patient's platelets were defective in the production of thromboplastin. This abnormality was demonstrated on three separate occasions:

Date	Incubation-time (mins.)	1	2	3	4	5	6
Feb. 25	Clotting-time (secs.)						
	Control platelets	32	15	10	8	8	9
	Patient's „	60	60	45	40	30	24
Feb. 27	Control platelets	60	17	10	10	11	11
	Patient's „	70	65	60	45	40	40
March 3	Control platelets	38	16	10	8	7	8
	Patient's „	65	60	50	45	43	38

The patient's plasma and serum formed normal amounts of thromboplastin with control platelets.

A diagnosis of non-thrombocytopenic purpura or thromboasthenia was therefore made.

Treatment

The patient had a cervical dilatation and a uterine curettage; radium 50 mg. was inserted into the uterine cavity for 40 hours. The curettings were of normal secretory endometrium. (Dr. H. R. Harris.)

Discussion

Stefanini and Dameshek (1955) suggest that platelet dysfunction is probably more common than appears from the published accounts. Biggs and Macfarlane (1957) state that thromboasthenia may be hereditary or acquired; the latter can sometimes be explained on the basis of a coexistent blood dyscrasia—e.g., leukæmia or polycythæmia—or it can be secondary to " toxic damage ". In the case described above, the uterine hæmorrhage appears to be due to defective platelet function, but no initiating factor could be found.

In the light of recent observations on the changes in the blood during the normal menstrual cycle (Salvidio 1954, de Nicola et al. 1954, de Nicola 1954), one might postulate that the change in function of the platelets was initiated by an endocrine imbalance. A more detailed and thorough hæmatological investigation of the patients presenting with a dysfunctional uterine hæmorrhage will be required if any advance is to be made in understanding the pathogenesis of menorrhagia.

My thanks are due to Mr. Percy Malpas of the Women's Hospital, Liverpool, for permission to publish this case, and to Dr. W. R. Pitney, hæmatologist to the Royal Perth Hospital, Western Australia, for his help and criticism.

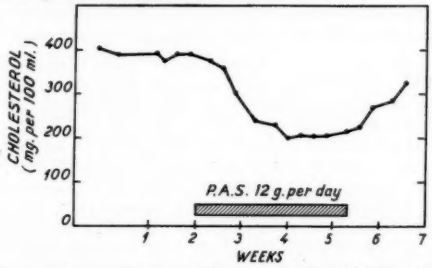
REFERENCES

Ackroyd, J. F. (1949) *Clin. Sci.* **7,** 231.
Biggs, R., Douglas, A. S. (1953) *J. clin. Path.* **6,** 23.
— Macfarlane, R. G. (1957) Human Blood Coagulation and its Disorders. Oxford.
Bonnin, J. A. (1956) *Brit. J. Hæmat.* **2,** 160.
Braunsteiner, H. (1955) *Wien. Z. inn. Med.* **36,** 421.
Buxton, C. L. (1941) *Amer. J. Obstet. Gynec.* **42,** 502.
Dameshek, W., Rheingold, J. J. (1949) *J. Amer. med. Ass.* **139,** 993.
de Nicola, P. (1954) *Rev. Hémat.* **9,** 536.
— Rosti, P., Carcupino, C. (1954) *Schweiz. med. Wschr.* **39,** 1130.
Ivy, A. C., Nelson, D., Bucher, G. (1940) *J. Lab. clin. Med.* **26,** 1812.
Lee, R. I., White, P. D. (1913) *Amer. J. med. Sci.* **145,** 495.
Quick, A. J. (1935) *J. biol. Chem.* **109,** 73.
— (1951) The Physiology and Pathology of Hæmostasis. London.
Salvidio, E. (1954) *Acta Hæmat.* **11,** 301.
Stefanini, M., Dameshek W. (1955) The Hæmorrhagic Disorders. New York.

Preliminary Communication

EFFECT OF *p*-AMINOSALICYLIC ACID ON SERUM-CHOLESTEROL

DURING a study of serum-cholesterol levels in various types of patient it was noted that antituberculous treatment in most cases reduced the concentration of lipoids in serum considerably. This effect proved to be due to *p*-aminosalicylic acid (P.A.S.). In 8 patients with pulmonary tuberculosis the serum-cholesterol averaged 245 mg. per 100 ml. (range: 145 to 316) before the treatment, and during the first eight weeks of treatment (including P.A.S. 12 g. per day) 180 mg. per 100 ml. (range: 113 to 252, twenty determinations). The lowest values generally were observed during the first month, but in 2 cases, followed for more than eight weeks (fourteen and twenty-two weeks) the serum-cholesterol remained about 30% lower than the initial values. Unesterified cholesterol showed the same relative changes as total cholesterol, whereas phospholipids and triglycerides, after a fall of about 35% during the first month of treatment, tended to return to pretreatment levels.



One patient with diabetic hypercholesterolæmia received 12 g. of P.A.S. daily for twenty-three days (see figure). A woman with coronary heart-disease received the same amount for ten days, after which the treatment was discontinued because of diarrhœa: her serum-cholesterol was reduced from 310 to 214 mg. per 100 ml. P.A.S. 6 g. daily was given for three weeks to 2 patients with essential hypercholesterolæmia, whose serum-cholesterol fell from 405 to 330 mg. and from 360 to 260 mg. The body-weight and basal metabolic rate of the patients did not change.

The serum-cholesterol-lowering effect of P.A.S. was unexpected, because P.A.S. is known to have anti-thyroid properties.[1] Apparently, however, serum-cholesterol remains normal or low, even in cases where P.A.S. causes myxœdema (cf. table I of Macgregor and Somner [2]; one case observed by us, unpublished). This phenomenon may throw light on the blood-cholesterol-regulating function of the thyroid gland.

Many problems remain to be solved before it can be decided whether P.A.S. is useful in the treatment of hypercholesterolæmia; but the effect on serum-cholesterol appears to be comparable to that obtained by known dietetic and medicamental procedures. The combination of a blood-cholesterol-lowering and a moderately anti-thyroid effect may be particularly desirable in coronary heart-disease.

The cholesterol determinations were performed by the Central Laboratory, Rigshospitalet.

NIELS TYGSTRUP, M.B.
KJELD WINKLER, M.B.
ERIK WARBURG, M.D.

Medical Department B, Rigshospitalet, Copenhagen

1. Clausen, K. H., Kjerulf-Jensen, K. *Nord. Med.* 1951, **45**, 475.
2. Macgregor, A. G., Somner, A. P. *Lancet*, 1954, ii, 931.

Reviews of Books

Preventive Medicine in World War II

Vol. 4. *Communicable Diseases transmitted chiefly through Respiratory and Alimentary Tracts.* Editor in chief: Colonel JOHN BOYD COATES, Jr., M.C. Washington: Office of the Surgeon General. 1958. Pp. 544. $5·50.

IN this interesting book the account of each disease traces its history as a military problem from the Revolution through the war between the States and the 1914–18 war to the present day. The editor admits that much of his material is statistical, and no-one knows better than he that the retrospective use of this has its dangers. The official methods of record-keeping have compelled him to use geographical divisions not designed for epidemiologists.

The concept of "common respiratory diseases" has been useful, and their high incidence when populations are mixed by the assembly of recruits is discussed imaginatively. The same phenomenon was seen, as might be expected, with meningococcal meningitis: the account of the natural history of this disease by J. J. Phair is probably the most complete (and most interesting) yet published. In the 1939–45 war diphtheria never became a nuisance until the occupation of Germany coincided with an epidemic among the civil population; but diphtheritic infections of wounds were not uncommon in the India-Burma-China and Pacific theatres. In the Pacific theatre 38% of one infantry regiment (about 2800 men) were found to be Schick-positive; active immunisation (with 10% severe reactions) abolished these infections. Streptococcal infections caused much delay in training. Prophylaxis with sulphonamides was successful initially (as it was always with meningococcal infections), but the development of resistant strains discredited this useful temporary measure. The incidence of rheumatic fever was always high compared with European experience, but acute nephritis does not get a mention.

A long section on the diarrhœal diseases contains two sections which are as important in peace as in war. The factors which influence the reporting of such ailments are varied and complex: an adequate laboratory service will not compensate for the natural human tendency to avoid the doctor if possible. Equally instructive is an analysis of these periods of a soldier's life when he is especially susceptible to intestinal infections: at camps under construction where water-supplies and sanitation are still incomplete; in training when he has yet to learn the art of field hygiene; in such places as coral atolls where classical conservancy methods are impossible; on first arrival in any country where such diseases are common; in troopships; and in a campaign of movement. The claim to have ended an epidemic of Sonne dysentery by the removal of a carrier or two is made once or twice, whereas recent experience shows that the so-called carrier is harmless: the epidemic ends whether he is moved or not.

This is a book to be read carefully by every epidemiologist. It is full of odd information, always well documented, and thoughtful commentary. One aspect is somewhat alarming. Every soldier must try to guess the conditions of the next war—if there must be one—and it is now argued that this would be a short mobile war of survival. Prevention of disease depending on extensive sanitation or numerous laboratories is probably to be equated with cavalry and the Gattling gun: the emphasis must be on field hygiene at its simplest and on active immunisation.

Psychiatry and the Public Health

G. R. HARGREAVES, Nuffield professor of psychiatry, University of Leeds. London: Oxford University Press. 1958. Pp. 118. 12*s.* 6*d.*

To the inquiring mind, one of the most stimulating things about psychiatry is the breadth of its territory and its impingement on so many others. Admittedly the frontiers are vague and somewhat embattled, and the territory itself is clothed in mist; but the landmarks that seem to be emerging should be sufficient encouragement to the doubtful explorer. In this series of interesting lectures delivered to the London School of Hygiene and Tropical Medicine, Professor Hargreaves discusses in

broad terms the relation of psychiatry to the public health. He traces very briefly the historical development of psychiatry and the origins of the concept of " mental hygiene " and then goes on to discuss psychiatric institutions, administration, some social aspects, the role of the general practitioner, and finally the relation to the practice of public health.

The material is well presented and stimulating. It seems to represent Professor Hargreaves' random reflections rather than a planned statement on preventive psychiatry; but it is perhaps none the worse for that. He does not discuss, for example, the idea of a " medical officer of mental health ", nor the increasing preventive practice in the U.S.A. of " mental check-ups ". The academic reader will regret the absence of an index and references, and the author might have been expected to mention the important association between unfavourable social conditions on the one hand and mental disease and crime on the other. Moreover, it is odd to see the pros and cons of medical superintendents argued out in such a work. But it is all good reading.

Head Injuries

E. S. GURDJIAN, M.D., professor of neurological surgery; J. E. WEBSTER, M.D., associate professor of neurological surgery, Wayne State University College of Medicine, department of neurosurgery, Grace and Detroit Memorial Hospitals. Boston: Little, Brown. London: J. & A. Churchill. 1958. Pp. 482. 100*s*.

THIS comprehensive, lucid, and reliable book covers every aspect of head injuries. The complications are described precisely; and the pages are studded with details and accurate observations, with a fine appreciation of the relative importance of symptoms and signs, and descriptions of rarities which will gladden the heart of anyone dealing with many head injuries. No such work as this can please everyone in every detail. The analysis of rotational mechanical forces is given no prominence; the classical paper by Denny-Brown and Ritchie Russell is mentioned only briefly, and the demonstration of rotational forces by Holbourn not at all. In this regard our hands know instinctively what our minds may forget. If a child's plaything, a globe containing water with a miniature snow-scene in it, is handed to anyone, his hand will not waste energy in shaking it in a linear fashion, but will immediately rotate it.

This volume, the fruit of wide and long experience, can be recommended to young surgeons; and it will be read with profit and pleasure by their elders.

Lesions of the Lower Bowel

RAYMOND J. JACKMAN, M.D., M.S., associate professor of proctology, Mayo Foundation Graduate School, University of Minnesota, Rochester, Minnesota. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1958. Pp. 345. 117*s*.

THIS book is clearly founded on a great deal of clinical and teaching experience, and the author's conclusions will be of interest to British proctologists. On controversial subjects, such as the prognosis of polyps, he tends to adopt a sensible compromise attitude. There is similar common sense about many simple therapeutic measures he recommends; and most readers will regret that he has not described in fuller detail the methods and results of treatment at the Mayo Clinic. The coloured illustrations of proctoscopic findings are a credit to him and his publishers, but it is doubtful whether even the best pictures can be of more than marginal help to the aspirant proctoscopist.

Operative Surgery (Progress vol. 1 and general index. London: Butterworth. 1958. Pp. 185. 60*s*.).—With the index to this eight-volume work, edited by Prof. Charles Rob and Mr. Rodney Smith, the publishers have introduced the first progress volume. They intend to keep the main work up to date by means of periodical publications of this kind, though on this occasion it appears that the opportunity has been taken to repair some previous omissions.

An Introduction to Pathology (3rd ed. London: Longmans Green. 1958. Pp. 660. 45*s*.).—The latest edition of this deservedly popular " Introduction " by Prof. G. Payling Wright maintains the high standard of its predecessors. The text, references, and illustrations have been carefully revised. The author is punctilious in providing evidence for his assertion of facts, and with equal care he denotes beliefs that are too readily accepted as facts. Those reading this book may regret that it stands alone without a companion volume on " special " pathology.

Modern Chemotherapy of Tuberculosis (New York: Medical Encyclopedia Inc. 1958. Pp. 109. $4).—Dr. Roger Mitchell and Dr. J. Carroll Bell have produced an easily read and valuable monograph (no. 11 in the Antibiotics Monograph Series). There is still controversy about drug regimens, and it would be possible to take issue with them at some points, particularly in relation to intermittent administration of streptomycin and the dosage of isoniazid; but the book should not be judged by insular prejudices. It is well documented, which may be both an asset and a liability. On the one hand this provides a valuable source of reference; on the other hand, the work tends here and there to give a somewhat uncritical list of published reports. But this is a minor fault, and it is well worth reading for its lucidity and wide range.

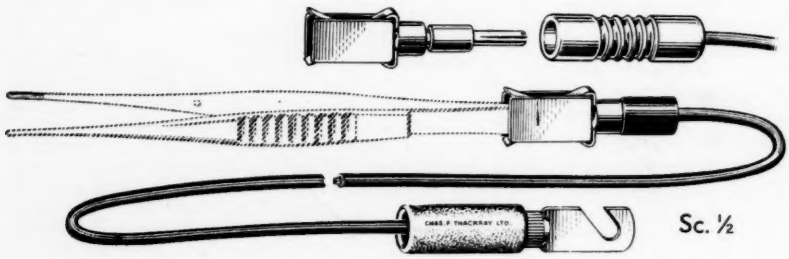
Black's Medical Dictionary (23rd ed. London: A. & C. Black. 1958. Pp. 1013. 35*s*.).—In preparing this new edition Dr. W. A. R. Thomson has rewritten many of the entries and has added many new sections, including notes on steroid anæsthetics, artificial insemination, carbutamide, corneal grafting, Coxsackie viruses, hyaline membrane disease, laryngotracheobronchitis, neomycin, prednisone and prednisolone, and tranquillisers.

New Inventions

UNIVERSAL DIATHERMY ADAPTOR

THE universal diathermy lead attachment is an adaptor which enables any pair of forceps to be used with diathermy. It consists of a small rectangular metal box with attached lead and clip for connection to the diathermy machine, or with adaptor for attachment to an existing lead.

The box end fits snugly over the head of the forceps, and is held firmly in position by three strong springs. The lead is plugged into the machine, converting the attached instrument into a diathermy forceps. The current is controlled by the operator using the foot switch; thus bleeding points can be dealt with quickly and easily.



Sc. ½

The adaptor, which is very light, and simple to use, obviates the need to have a special pair of hæmostats or forceps solely for diathermy. Long or short forceps can be clipped on at will, and good control is always obtained, without sparking.

It was made for me by Messrs. C. F. Thackray, 38, Welbeck Street, London, W.1, from whom it may be obtained.

Putney Hospital, London, S.W.15 J.-C. GAZET F.R.C.S.

THE LANCET

LONDON 7 MARCH 1959

Hæmatoma by Dialysis

WHEN it became clear that the original conception of chronic subdural hæmatoma as a complication of trauma was correct, it seemed that the condition should be simple enough to understand. The rather mysterious notion of pachymeningitis hæmorrhagica interna, described by VIRCHOW among others, was generally dropped. Further studies have confirmed the high incidence of recognised trauma, and have shown that, where no history of trauma is obtained, this is often because the injury was trivial or it affected the mental state. NORDLIE [1] points out that the diagnosis can now be made so accurately that it is no longer reasonable to speak of an "exploratory burr-hole". Nevertheless, GROFF and GRANT [2] maintained that "the origin and cause for the development of subdural hæmatomas remain enigmatic", and there is still some reason for this view. What is especially unclear is why the subdural hæmorrhage which causes symptoms in the acute stages does not usually go on to form a chronic subdural hæmatoma. Admittedly, an acute hæmatoma is often accompanied by serious brain damage and has a high mortality, but the survivors do not suffer from chronic hæmatoma. Acute subdural hæmatoma is caused daily by intracranial operations, yet in such cases subsequent operation for removal of chronic subdural hæmatoma is virtually never needed. NORDLIE suggests that acute and chronic subdural hæmatoma are two completely different conditions, but he does not explain how the difference arises. MUNRO [3] has put forward the view that a tear in the arachnoid at the time of the original injury leads to admixture of cerebrospinal fluid (C.S.F.), which accounts not only for the liquid nature of the hæmatoma but also for its appearance occasionally as clear yellow fluid (hygroma), and for the characteristic clinical picture. This view, though it does explain the hygroma rather well, has not been generally accepted; for it fails to account for one important fact—that the liquid blood in a subdural hæmatoma is free from fibrinogen. Round the edges of the hæmatoma lies solid clot in which the fibrin is; and apparently movement of the brain inside the skull causes the fibrin to become entangled there and over the internal and external surfaces, leaving a liquid centre which gradually swells by osmosis as molecules break down into smaller size and increase in numbers. GARDNER [4] demonstrated the formation and expansion of hæmatoma by implanting 'Cellophane' bags filled with blood in the subdural space of animals.

But, convincing as this work is, it fails to explain why the known acute subdural clot does not invariably undergo these changes. The explanation may be that such changes usually complicate venous bleeding only if the brain is small in relation to the cranium. Otherwise the hæmatoma is absorbed—except very occasionally in young patients where it gives rise to high intracranial pressure.

The manifestations of chronic subdural hæmatoma are notoriously varied. In rather over half the cases, a history of trauma is obtainable when the patient is first seen; the proportion with a positive history rises later owing to more accurate recollection in patients who have recovered. Commonly, there is a latent interval—usually of between two and six weeks, and occasionally as long as four months. This latent period, which in retrospect may not be completely symptom-free, merges into a period during which recurrent headaches (particularly in the mornings), giddiness, attacks of "falling about", vomiting, and fluctuating drowsiness may be noted. Some patients are admitted to hospital with urinary retention, bowel obstruction, or fracture.[5] Sometimes there is simply progressive mental and nutritional deterioration—a failure to thrive. At this stage abnormal physical signs are often slight: there may be visible strabismus, a characteristic mild confusion especially about the past, signs of pyramidal disturbance in the form of either frank hemiparesis or hypertonicity, or an extensor plantar response. If the disorder is not diagnosed and treated at this stage, the signs and symptoms progress and the patient eventually passes into coma, when only disturbance of the ocular muscles or pyramidal signs may suggest the correct diagnosis; but a large proportion of patients are said to die suddenly and unexpectedly. The pupils may be almost normal, and the pupil on the contralateral side may be the larger. Focal epilepsy, speech disturbance, and other clear localising features are unusual. Papillœdema is inconstant, and indeed the C.S.F. pressure may be high, low, or normal; xanthochromic fluid with a high protein content is characteristic but not invariably found. Hygroma may produce intermittent pyrexia and occipital headache with nuchal rigidity. The diagnosis used to be routinely confirmed by exploration, although air encephalography occasionally revealed a hæmatoma; and it used to be said that no patient should die in undiagnosed coma without exploratory burr-holes having been made. Nowadays, by means of angiography the diagnosis in most cases can be confirmed before exploration if the urgency is not too great. The angiographic picture is highly characteristic. Electroencephalography has not proved particularly helpful in this condition; slow waves may be found, notably on the side of the lesion, suggesting disturbance of cerebral function due to compression of the brain. The voltage of slow or fast waves has been noted to be lower on the side of the lesion; indeed, flattening has been regarded as the most significant localising feature.[6–8]

1. Chronic Subdural Hematoma. By RAGNAR NORDLIE. Oslo: Johan Grundt tanum Forlag. 1958. Pp. 164.
2. Groff, R. A., Grant, F. C. *Surg. Gynec. Obstet.* 1942, **74**, 9.
3. Munro, D. *New Engl. J. Med.* 1942, **227**, 87.
4. Gardner, W. J. *Arch. Neurol. Psychiat.* 1932, **27**, 847.
5. Stuteville, P., Welch, K. *J. Amer. med. Ass.* 1958, **168**, 1445.
6. Jasper, H. H., Kershman, J., Elvidge, A. *Arch. Neurol. Psychiat.* 1940, **44**, 328.
7. Sullivan, J. F., Abbott, J. A., Schwab, R. S. *Electro enceph. clin. Neurophysiol* 1951, **3**, 131.
8. Williams, D., Reynell, J. *Brain*, 1945, **68**, 123.

The lesion is treated by evacuation through one or more burr-holes; but the death-rate after operation is far from negligible, and recovery may be incomplete,[9] especially in the very elderly. Residual symptoms include confusion, personality disorder, hallucinations, Korsakoff's psychosis, dementia, and locomotor disability. Mental abnormalities may develop after the hæmatoma has been treated surgically. The cause of incomplete recovery has sometimes been believed to be cerebral œdema,[10 11] but this view is not supported by much evidence. Most of the patients who do badly continue to have a low C.S.F. pressure; many workers believe that this is associated with dehydration.[12 13] Atrophy may result from compression of the brain or from ischæmia due to compression of the vessels, and both processes may be increased by dehydration—either coincidental or therapeutic. Treatment may be made more effective by carefully washing the cavity, by filling it with saline solution, and by closing the wound with the head low. The compression seldom gives rise to classical uncal herniation.[14] Attempts to elevate the base of the brain by injecting saline solution intrathecally, and to expand the brain by intraventricular injection, have not secured universal approval.

In infants atrophy of the brain is especially liable to develop. Sometimes removal of the inner membrane may be necessary to allow the growing hemisphere to expand [15]; but this is not always necessary or successful, for in many cases expansion takes place perfectly well after treatment by aspiration and washing out, while in others, even after removal of membrane, expansion does not occur. If fractional evacuation, followed by drilling of burr-holes with washing out of the cavity, does not procure expansion, it would seem reasonable to follow Ingraham's [15] advice to remove any distinct inner membrane—and to examine for microgyria.

Enzymes in the Blood

THE subject of enzymes in the blood is of interest to clinical investigators; for estimations of serum alkaline and acid phosphatases have long been used in the study of liver and bone diseases and of prostatic neoplasms, serum-transaminase estimations are now being used as an index of myocardial, hepatic, and muscular disorders [16]; and a specific stain for alkaline phosphatase in polymorphonuclear leucocytes has been introduced to distinguish between leukæmia and a leukæmoid reaction.[17] A conference was held by the New York Academy of Sciences [18] in order to show clinical investigators what enzymologists are doing, and enzymologists what clinicians are interested in; but in fact most of the papers presented were biochemical and biophysical rather than clinical.

GROSS and MARKS [19] drew attention to a hereditary deficiency of the red-cell enzyme glucose-6-phosphate dehydrogenase which is associated with susceptibility to hæmolytic anæmia after certain drugs—for example, the urinary antiseptic, nitrofurantoin. GRANICK and MANZERALL [20] are investigating the red-cell enzymes that are responsible for porphyrin synthesis and have shown how these complex ring compounds can be synthesised from glycine and succinate. SCHULMAN et al.[21] surveyed the possibility of using phosphatides in place of blood-platelets for blood-coagulation studies. They dealt particularly with cephalin made from soybean, which, they suggest, may also be useful in the control of bleeding due to thrombocytopenia; it has been given to patients with apparent benefit and no unpleasant side-effects. THIERS and VALLEE [22] described their "coenzometer"—a relatively simple instrument that can be used in clinical laboratories for the determination of serum enzymes, and they made some critical remarks about misleading methods of estimating serum enzymes that have become popular. HAUSS and LEPPELMANN [23] pointed out that changes in serum-glutamic-oxalacetic-transaminase and some other serum enzymes are found not only in acute myocardial infarction but also in an "acute syndrome" in the course of infectious diseases and after surgical operations. WOLFSON et al.[24] suggested that estimation of serum-isocitric-dehydrogenase will distinguish acute viral hepatitis from other liver diseases causing jaundice, such as obstructive jaundice and metastatic carcinoma of the liver. KRETCHMER et al.[25] illustrated the effect of hereditary enzymatic disorders by the case of a 4-month-old infant with hypophosphatasia.

The remaining three-quarters of the papers in this symposium are unlikely to interest clinical investigators in general. For this there may be several reasons. Presumably one is the old opposition between pure and applied science: some of these papers are about matters of absorbing interest to enzymologists, but do not seem to have any connection with disease in man apart from the fact that they are studies of blood. Another difficulty is incomprehensibility: technical jargon with plenty of initial abbreviations is employed too often and means little to those not working in enzyme chemistry. Furthermore the papers of many of the workers in this collection give the impression that the investigation was designed without regard to what their clinical colleagues wanted. This is very evident in the section on white-cell enzymes, in which many investigators lump together all "leucocytes", irrespective of the fact that neutrophil granulocytes, lymphocytes, and monocytes—to mention only the three main types—are known to have different metabolic activities. Thus BECK,[26] investigating leucocyte glycolysis, found distinct differences between the aerobic glycolytic rates of normal leucocytes, those of chronic

9. Davies, F. L. *Proc. Soc. Brit. neurol. Surg.* December, 1958.
10. Tönnis, W. *Zbl. Chir.* 1934, **61**, 2548.
11. Kunkel, P. A., Dandy, W. E. *Arch. Surg.* 1939, **38**, 24.
12. Sjöqvist, O., Kessel, A. *Arch. klin. Chir.* 1937, **189**, 482.
13. Hanke, H. Das subdurale Hämatom. Berlin, 1939.
14. Small, J. M. *J. Neurol. Neurosurg. Psychiat.* 1958, **21**, 232.
15. Ingraham, F. D., Matson, D. D. *J. Pediat.* 1944, **24**, 1.
16. *Lancet*, 1958, ii, 1318.
17. Leonard, B. J., Israëls, M. C. G., Wilkinson, J. F. *ibid.* 1958, i, 289.
18. Enzymes in Blood. *Ann. N.Y. Acad. Sci.* 1958, **75**, pp. 1-384. Consulting editor LAURENS P. WHITE. $5.00.
19. Gross, R. T., Marks, P. A. *ibid.* p. 106.
20. Granick, S., Manzerall, D. *ibid.* p. 115.
21. Schulman, I., Currimbhoy, Z., Smith, C. H., Erlandson, M. E., Schorr, J. B., Fort, E., Wehman, J. *ibid.* p. 195.
22. Thiers, R. E., Vallee, B. L. *ibid.* p. 214.
23. Hauss, W. H., Leppelmann, H. J. *ibid.* p. 250.
24. Wolfson, S. K., Spencer, J. A., Sterkel, R. L., Williams-Ashman, H. G. *ibid.* p. 260.
25. Kretchmer, N., Stone, M., Bauer, C. *ibid.* p. 279.
26. Beck, W. S. *ibid.* p. 4.

myelocytic leukæmia, and those of chronic lymphatic leukæmia; the respective rates of lactic-acid production from glucose were 45, 13·2, and 4·8 μmoles per 10^8 cells per hour. BECK has found that the differences are due to deficiency of hexokinase " in leukemic cells ". But he does not mention the fact that functioning neutrophil polymorphs make up 60% or so of normal leucocytes, a much smaller proportion of leucocytes in chronic myelocytic leukæmia, and perhaps not more than 1% in chronic lymphatic leukæmia. The fact that the patients had leukæmia may have nothing to do with his results, for which hexokinase in neutrophil polymorphs may have been responsible. Clinical hæmatologists would not consider " leucocytes " as a single entity, and perhaps if they had been consulted before the work began this pitfall would have been avoided. It is admittedly difficult to separate the different types of leucocyte, and for this reason histochemical techniques such as the alkaline-phosphatase stain for granulocytes are being developed.

Enzyme studies have already produced helpful clinical diagnostic tests and provided the clue to some mysterious diseases such as von Gierke's glycogen-storage disease, phenylpyruvic oligophrenia, and galactosæmia. But L. P. WHITE, introducing the report of the New York meeting, says: " It is, however, a sad reality that enzymologists and clinical investigators do not usually communicate with each other at any level more basic than that of casual social intercourse." If this situation is to be remedied (and it does not apply only to enzymology) then surely enzymologists should be willing to explain in understandable terms what they are doing and to what end, and the clinical investigator should be willing to explain equally clearly what he would like to know and why. This report shows that we have still a long way to go.

The Age for Motherhood

MOTHERHOOD resembles a typical athletic performance in at least one respect—the capacity to undertake it efficiently falls off very rapidly with age. BAIRD et al.[1] have analysed birth records for the city of Aberdeen by maternal age, social class, and parity, with some striking results. It is difficult to isolate the maternal age factor in such series, because age at first conception depends on social status, and because within a social class the careless, the feckless, and the unintelligent are traditionally assumed to be most easily " caught "; but both these biases would tend to improve the chances of successful maternity for the late-marrying. In fact, for each social class the stillbirth-rate rises exponentially from the age of 15, with a doubling time of about 18 years—the curves for social classes I with II, III, and IV with V are almost evenly spaced. Very few of the mothers who had their first baby before the age of 20 came from classes I or II, and their physical health and stature were inferior to those of their better-off but later-reproducing neighbours. They also tended, in terms of appearance, to age early: " it is by no means uncommon to see a primigravida of 22 who has lost all the bloom of youth and who could easily be taken for a woman in her late twenties or early thirties ". While all the class-specific infant and maternal mortalities have fallen they show no tendency for the classes to attain parity. But a young mother of class IV–V still has a biological advantage compared with a 35-year-old primipara of class I which money cannot replace.

This large social factor—which is present in almost all health statistics of this kind—is enough to dispel facile optimism about the Welfare State. But it is less remarkable biologically than the rate at which the performance of all classes deteriorates with age at first parity. Of mothers under 20, 80% are spontaneously delivered in less than twenty-four hours, compared with 25% aged 35 or more. Efficiency of lactation behaves in exactly the same way. The frequency of ectopic implantation and of placenta prævia and the need for episiotomy also rise steadily with age at first parity (eclampsia does not seem to be affected). From the figures it is evident (as most midwives have long known) that the chance of a successful outcome to a first labour declines notably with every year that it is postponed after puberty, and would do so even more conspicuously if there were no penalty-selection of youngest mothers.

The case of the late primipara is not a simple example of senescence, like the smaller decline in reproductive efficiency with age when parity is ignored. It is a type of disuse-senescence, and BAIRD et al. point to the other gynæcological penalties of infertility, such as fibroids. The important thing is to start early, and postponement of first labour must in itself be the cause of quite a sizeable section of the residue of maternal and fœtal losses.

This stressing of a fact which has long been known is valuable. But it is difficult to see what, in a real society, can be done about it beyond counselling married couples who intend to have children to do so early—desirable advice in any event, in case their fertility is low. Propaganda for early marriage, which may be desirable on other grounds, is beside the point here; for such propaganda is not certain, given present trends, to have any substantial effect on the age of the first intentional pregnancy. In our society any considerable changes in patterns of sexual behaviour with age are now likely to derive directly from the availability of contraception. In proportion as it relies on more technology requiring long training, and as it prolongs education into adult life, our culture is much more likely to discourage early motherhood. Medical men have faced this problem themselves longer than anyone. Marriage among students, and even (in view of the steady fall in the age of puberty) among high-school pupils, has sometimes found advocates; but, if they are to be parents as well, we might have fewer obstetric casualties now at the cost of more psychiatric problems in the next generation, brought up by part-time parents in provisional homes. In America, where courtship begins in childhood and marriage is not unduly late, parental immaturity is still a major problem of preventive psychiatry in couples aged 30. Nor are we likely to overcome the

1. Baird, D., Hytten, F. E., Thomson, H. M. *J. Obstet. Gynæc. Brit. Emp.* 1958, **65**, 865.

logistic and economic difficulties as Romans or 14th-century Englishmen did, by marrying our 13-year-old daughters to grown men: the age-discrepancy has become culturally offensive even if it is biologically defensible.

It might, however, be worth ensuring that the extent of the penalty against late primiparity is understood, so that people can weigh it in planning their lives. Life, for most people, passes remarkably fast, even without the intervention of wars or separations; and, without exercising improper pressure, the family doctor is sometimes doing his patient a favour by pointing this out.

Annotations

ANTIBIOTICS: NEW DISCOVERY

AN important event in the development of antibiotics is reported by Batchelor, Doyle, Naylor, and Rolinson.[1] Working in the microbiological unit of Beecham Research Laboratories, they have isolated 6-amino-penicillanic acid, from which any number of new penicillins may be obtained. In this investigation they have had the advantage of discussions with Prof. E. B. Chain, Sir Ian Heilbron, and Dr. A. H. Cook, each of whom was involved in the early work on penicillin. In view of the history of penicillin, it is particularly gratifying that this new break-through is also a British achievement.

The consequences could be far-reaching. Already there are indications that it will be possible to produce readily penicillins which do not cause reactions in penicillin-sensitive patients, such as penicillin O (allylmercapto methyl penicillin),[2] and cephalosporin N (α-amino adipic penicillin).[3] New approaches to the problems of the resistant staphylococcus should now be feasible, and means may be found for enhancing the activity of penicillin-type compounds against gram-negative bacteria.[4]

Though new antibiotics are reported every year, these have all been obtained by microbiological fermentation—except the relatively simple chloramphenicol, which, though first made by fermentation, is now made synthetically. The chemical synthesis of penicillin V by Scheehan and Henery-Logan [5] is adaptable to the synthesis of unnatural penicillin-like antibiotics, but the isolation in quantity of 6-amino-penicillanic acid will make such compounds readily available on a commercial scale.

SECOND COLLEGE COLLOQUIUM

WORDS are not like coins—they can be spent without causing any apparent deficit. This is an age of almost competitive communication, and the post-war scene has been lit by many gatherings called to serve this purpose. Leaving aside the large international congresses, already established before the war, and now almost outgrowing their usefulness, we have two main types of colloquium—the one where a small group of experts, often from different disciplines, meet to discuss a limited subject; and the other where the main purpose is the sharing of special knowledge and experience with a wider group. In America specialists of all kinds are already inured to ordeal by panel discussion, but here this second type of colloquium is a comparative innovation. For such a conference, opening speakers of high competence and authority are one of the essentials; and any single medical school, however talented, may find this a difficulty. By calling in outsiders to fill gaps, some have achieved great success: for example, several valuable conferences have been held at the Postgraduate Medical School of London. Last year the Royal College of Physicians, acting through its postgraduate committee, set out to meet in this way one of the needs of the many hospital physicians who want to keep in close touch both with one another and with the advances which make today's medicine so exciting. The college's first colloquium, on anæmia and the alimentary tract,[1] was a great success; and on Feb. 27–28 it was followed by the second, on the clinical effects of electrolyte disturbances.

The first morning, with Prof. Robert Platt, the president, in the chair, was given to the physiology and methods of study of electrolyte problems, and to the genesis and treatment of œdema. In the afternoon, wher. Dr. E. N. Allott took the chair, renal failure and potassium depletion were discussed. The second day, under the successive chairmanship of Prof. R. A. McCance and Dr. H. L. Marriott, was allotted to the electrolyte aspects of a number of clinical problems: endocrine disorders, including Addison's disease, aldosteronism, and diabetes; gastrointestinal disorders; heart-failure; and the period after trauma or operation. As in the previous colloquium, the President had been advised in his choice of speakers by a small group—in this case Prof. M. L. Rosenheim, Prof. D. A. K. Black, and Dr. R. I. S. Bayliss—and the invited speakers had been sent a short statement explaining the scope and object of the meeting. Perhaps because of these preparatory steps, the papers were of a high and uniform standard: indeed, the occasion was one of those when "all rowed fast but none so fast as stroke". It may be wrong to particularise: but those who heard them will long remember the lucid and methodical way in which Dr. H. E. de Wardener outlined the means of distinguishing between diabetes insipidus and compulsive drinking; the careful approach of Dr. Victor Wynn and Dr. D. S. Munro—in contrast to the constructive speculation of Prof. G. M. Bull—in search of a volume receptor; the minute attention paid by Prof. C. E. Dent to the technique of balance studies; and Dr. M. D. Milne's characteristic and stimulating account of aldosteronism. Everyone enjoyed the little tussle in which Dent and Reifenstein (in absentia) argued with Milne and Descartes (also in absentia) whether positive balances should be charted above or below the zero-line.

After each small group of opening papers, there was time for general discussion. Many physicians took part in this, recounting their own experience, or asking advice on practical problems. Sometimes the opening speakers came back at one another; and this too can be instructive, even if only to show that expertness does not guarantee a just proportion between emotional heat and intellectual light. On the whole, a nice balance was struck between the conflict of experts and the faithful replies to "bread and butter" questions—not all of them easy to answer.

Those who attended this colloquium seemed in no doubt that it had repeated the success of the one before, and the announcement that the series will continue was welcomed. The plan is that colloquia should be held at

1. Batchelor, F. R., Doyle, F. P., Naylor, J. H. C., Rolinson, G. N. *Nature, Lond.* 1959, **183**, 257.
2. Ford, J. H., Churchill, B. W., Colingsworth, D. R. *Antibiot. & Chemother.* 1953, **3**, 1149.
3. Abraham, E. P. Biochemistry of some Peptide and Steroid Antibiotics; p. 57. New York, 1957.
4. *ibid.* p. 61.
5. Scheehan, J. C., Henery-Logan, K. R. *J. Amer. chem. Soc.* 1957, **79**, 1262.

1. *Lancet*, 1958, ii, 255.

intervals of about eight months; and this planned non-conformity to the calendar should ensure that nobody will be repeatedly debarred from attending because they always clash with his busiest month—or, for that matter, his annual holiday. Like all good conferences last week's was oversubscribed; it was attended, after a ballot, by 120 people. Those who could not be there will be glad to know that the proceedings, including the discussions, are to be published with little delay.

PROTECTION AGAINST THE STREPTOCOCCUS

IN an important controlled study, Mortimer et al.[1] have found that penicillin administered intensively for six weeks to patients with rheumatic fever apparently reduces the likelihood that valvular heart-disease will be present a year later; the penicillin had no detectable effect on the acute manifestations, and Mortimer et al. suggest that the living streptococcus continues to play a significant part in the development of valvular disease even after symptoms of rheumatic fever have developed.

The case for continuous penicillin prophylaxis against streptococcal infections in patients who have had rheumatic fever has been solidly endorsed by experience, particularly since the American Heart Association's recommendations, now well known, were published in 1953.[2] Many thousands of rheumatic children and young people in the United States, and an increasing number in this country, have received and are receiving this protection.

Miller et al.[3] in Boston, Mass., made monthly observations (supplemented by home visits) over a three-year period on 235 healthy children—the siblings of 114 rheumatic-fever cases under outpatient care and prophylaxis. During this period these siblings had 603 respiratory illnesses, of which 76 (14%) proved to be group-A hæmolytic streptococcal infections. In 81 children without symptoms throat swabs were positive for group-A streptococci at some time during the study; and, although all streptococcal infections were adequately treated with penicillin, both in the group with symptoms and in the group without symptoms 40% showed antistreptolysin-O titre responses. It is thus clear that these patients who had had rheumatic fever were exposed at home to considerable opportunities for streptococcal infection. Even the symptom-free " carriers " among the families must have contributed significantly to the streptococcal environment—although, as Holmes and Williams [4] have suggested, such people probably disseminate fewer (and perhaps less dangerous) streptococci than those with frank acute streptococcal pharyngitis. Nevertheless, in this potentially infective domestic environment the prophylaxis which the rheumatic patients received was really protective. Their infection-rate with streptococci was less than a quarter of that in their unprotected brothers and sisters; and there were only 2 recurrences of rheumatism throughout the study.

At school the need for protection may be even greater, since the " carrier "-rate may be higher still, and here, as in other large communities, there are more potential sources of infection: Dr. Taylor and Dr. McDonald [5] have lately described an epidemic in the R.A.F. of group-A streptococcal infection which was apparently milkborne.[4] In a survey of streptococcal infection in a school population in Philadelphia, Cornfeld et al.[6] found that during a school year as many as half the children may have throat or nose swabs positive for group-A streptococci, even though the rate of clinical infection remains quite low. They found, moreover, that this state of affairs was not very much improved by intensive penicillin treatment of those harbouring the organism. It is wise to assume that in this country similar epidemiological considerations still apply; a survey of healthy schoolchildren in 1954 [7] certainly indicated as much. Streptococci remain a considerable feature of our bacterial environment; and children with a history of rheumatic fever, whether in hospital, at home, or at school, are receiving less than adequate care if they are not continuously protected against the dangers of infection.

GLUCOSE AND SUCROSE

MORE than thirty years ago Bennett and Dodds [8] showed that large quantities of liquid glucose were well tolerated and readily assimilated when taken by mouth and were of considerable therapeutic value in certain pathological conditions. An extension of this earlier work is reported on p. 485. Sir Charles Dodds and his colleagues find that the oral ingestion of liquid glucose results in a rapid rise of blood-sugar, and, in this paper, they also make a comparison with dextrose and sucrose.

For many years now, solutions containing glucose have been shown by clinical experience to be of some value in the ward and sickroom, especially in patients suffering from gastrointestinal disorders, febrile conditions, and liver disease (McDermott [9]). Solutions of glucose are a convenient way of providing, in an electrolyte-free medium, a substantial proportion of the daily calorie requirements of a resting patient. Here, the relative lack of sweetness of glucose makes it more likely to be accepted by the nauseated or anorexic patient.

The present paper by Dodds and his colleagues at the Courtauld Institute is of particular interest because the merits of glucose have recently been under discussion. In a report [10] issued last week, the Food Standards Committee concluded that, for oral administration, glucose has no physiological advantage over sucrose. This view, based on a scientific note reproduced as an appendix to the report, stems chiefly from the conclusion that sucrose can be metabolised more rapidly than can glucose when taken by mouth. The evidence for this opinion seems to be at variance with the most recent work of Dodds and his colleagues and is derived from work published many years ago by Higgins,[11] Deuel,[12] Deuel et al.,[13] Cole,[14] and Rabinowitch,[15] not specifically designed to solve the present problem.

It appears then, that the true value of the long-established use of glucose is still a controversial subject. Contradictions may conceivably have arisen through drawing general conclusions from the study of carbohydrate metabolism in particular diseases, and further evidence will be required.

1. Mortimer, E. A., Jr., Vaisman, S., Vignau, A., Guasch, J., Schuster, A., Rakita, L., Krause, R. M., Roberts, R., Rammelkamp, C. H. *New Engl. J. Med.* 1959, **260**, 101.
2. American Heart Association. *Lancet*, 1953, i, 285.
3. Miller, J. M., Stancer, S. L., Massell, B. F. *Amer. J. Med.* 1958, **25**, 825, 845.
4. Holmes, M. C., Williams, R. E. O. *J. Hyg., Camb.* 1958, **56**, 197, 211.
5. Taylor, P. J., McDonald, M. A. *Lancet*, Feb. 14, 1959, p. 330.
6. Cornfeld, D., Werner, G., Weaver, R., Bellows, M. T., Hubbard, J. P. *Ann. intern. Med.* 1958, **49**, 1305.
7. Holmes, M. C., Williams, R. E. O. *J. Hyg., Camb.* 1954, **52**, 165.
8. Bennett, T. I., Dodds, E. C. *Lancet*, 1925, i, 429.
9. McDermott, W. V. *Amer. J. Gastroent.* 1958, **30**, 51.
10. Ministry of Agriculture, Fisheries and Food. Food Standards Committee: Report on Soft Drinks. H.M. Stationery Office. 1959. (See p. 515.)
11. Higgins, H. L. *Amer. J. Physiol.* 1916, **41**, 258.
12. Deuel, H. J., Jr. *J. biol. Chem.* 1927, **75**, 367.
13. Deuel, H. J., Jr., Guilick, M., Butts, J. S. *ibid.* 1932, **98**, 333.
14. Cole, S. W. *Lancet*, 1935, i, 431.
15. Rabinowitch, I. M. *J. Nutr.* 1945, **29**, 99.

Animal experiments with ^{14}C-labelled sugars have advanced our understanding of carbohydrate metabolism, but the work from the Courtauld Institute has shown that there is still scope for the more traditional techniques. Advances can still be made in territories that appear at first sight to have been well explored.

A number of questions remain to be answered if the paradox is to be resolved. The present work shows that liquid glucose produces a rapid rise in blood-sugar, but it would be interesting to know the rate at which the sugars (or their metabolites) appear in the peripheral tissues. Such information would be useful in any consideration of the relative physiological merits of different sugars. Experiments designed to determine the proportion of a carbohydrate load utilised by the various tissues of the body would yield valuable information, and much more could be known about the effects of different pathological changes on carbohydrate handling. A closer study of the non-dextrose components of liquid glucose might also be rewarding, in view of the apparently rapid absorption.

BLOOD-TRANSFUSION ACCIDENTS

WHAT is an "incompatible" blood-transfusion, and how does it differ from a "hæmolytic transfusion reaction"? This question is prompted by a paper from Brooklyn which describes 30 patients who received "improper" blood. In this article Binder et al.[1] include among their incompatible transfusions 6 in which the donor blood was shown to be compatible in both the ABO and rhesus systems, though in 2 of these a hæmolytic reaction occurred in which no serological reason was discovered; they also include a 7th patient who was group-O Rh-negative and received group-O Rh-positive blood without developing any evidence of hæmolysis.

In Britain [2–4] and in France [5] a "blood-transfusion accident" is taken to include all damage to the patient caused by blood-transfusion, whatever the mechanism; a "hæmolytic transfusion reaction" implies hæmolysis in the patient's body, irrespective of the nature of the hæmolytic process; but "incompatibility" results from the interaction of erythrocytes with isoantibodies. Thus, Binder et al. have reviewed 27 blood-transfusion accidents, and 3 errors which seem to have had no detectable effect. Of the accidents, 25 proved to be serologically incompatible—23 in the ABO and 2 in the rhesus system. Of the 25 patients, 2 died from causes unrelated to the transfusion; but, of the total of 9 deaths, no fewer than 5 were associated with a severe hæmorrhagic state little affected by treatment.

Such a hæmorrhagic state, which has a poor prognosis,[5 6] is a known complication of incompatible transfusion; but a similar state may appear after transfusion of large volumes of apparently compatible blood.[7] The latter cause is better known in Britain, for it was only last year that the first case of death from the hæmorrhagic consequences of an incompatible transfusion was recorded.[8] In the Brooklyn series 3 patients received more than 9 litres of blood without effect on the bleeding; and it seems clear that neither fresh or stored whole blood, fresh-frozen or stored plasma, nor fibrinogen will combat the coagulation defect once this is established. Possibly this defect derives from the release of substances not usually regarded as being concerned with clotting; and of these the first which springs to mind is serotonin (5-hydroxytryptamine). This hormone has a strong and sustained constrictor effect on the renal vessels of rats, mice, guineapigs, rabbits, and dogs; and protracted perfusion produces patchy cortical necrosis. It has been suggested [9 10] that this cortical necrosis may be analogous to that in the kidneys of pregnant women who die after concealed accidental hæmorrhage; in this condition thromboplastins from the clotted blood escape into the general circulation and cause defibrination, and, since platelets are concerned in the clotting process, a large and sustained release of serotonin is likely to take place. The same mechanism might be involved in the transfusion cases. If this were indeed the case, it would be easy to demonstrate the increased urinary excretion of 5-hydroxyindole acetic acid in cases where urine is still excreted; and it might be worth treating such patients with a serotonin antagonist. But this hypothesis does not explain the apparent rarity of this complication in Britain.

Perhaps the most interesting part of the report by Binder et al. is their account of the errors which led to these accidents and the ineffectiveness of the methods proposed to prevent them. Special labelling, unit record numbers, printed labels in a colour code, and a system of transfer only on signature (all of which are now standard practice in Britain): these led to no improvement whatever—in fact, the figures for the last year were slightly worse than those for the first. Technical errors in the laboratory were responsible for only 8 cases, whereas 18 were due to errors of labelling, confusion between names, or interchange of sample tubes. Binder et al. suggest that this incidence of incompatibility—about 1 in 3000–4000 transfusions—is a minimum below which we are unlikely to go, because of human fallibility.

What is more to the point is their belief that more than half these tragedies occurred in cases where blood-transfusion was unnecessary:

> "... many transfusions are given without informed and thoughtful consideration of their need, or the possible utility ... of the plasma expander and vasopressor ... A more discriminating approach to blood transfusions would probably have decreased the incidence of reactions in other ways. Because the volume of blood expended would have been reduced, the incessant demands upon the blood bank for an immediate supply of blood would likewise have been diminished. The commonplace situation of the ward refrigerator full of blood would be lessened, and the possibility of inadvertent transfusion of another patient's blood would therefore be reduced. For these reasons the authors believe that the education of the responsible physician ... has the greatest potential for the ultimate reduction of incompatible blood transfusions."

This accords with the observations and opinions of more than one experienced British transfusionist.[11 12]

Surgeon Vice-Admiral Sir PERCIVAL NICHOLLS, medical director of the Navy from 1937 to 1941, died on March 1 at the age of 81.

1. Binder, L. S., Ginsberg, V., Harmel, M. H. *Surg. Gynec. Obstet.* 1959, **108**, 19.
2. Mollison, P. L. Blood Transfusion in Clinical Medicine. Oxford, 1956.
3. Discombe, G. *Lancet*, 1952, i, 734.
4. Discombe, G. *ibid.* 1954, ii, 936.
5. André, R., Dreyfuss, B., Salmon, Ch. Incidents et accidents de la transfusion sanguine. Paris, 1956.
6. Wiener, A. S. Blood Groups and Transfusion. Springfield, Ill., 1943.
7. Krevans, J. R., Bunker, D. P. *J. Amer. med. Ass.* 1955, **159**, 174.
8. Moore, J. F. *Brit. med. J.* 1958, ii, 1201.
9. Page, E. W., Glendening, M. B. *Obstet. Gynec.* 1955, **5**, 781.
10. Page, E. W. *Physiol. Rev.* 1958, **38**, 277.
11. Bowley, C. C., Darnborough, J. *Brit. med. J.* 1957, ii, 1432.
12. Discombe, G. Blood Transfusion. London, 1955.

The Wider World

ISRAEL
The Evolution of an Idea

HEDY SYMONDS
M.D. Vienna, M.R.C.S.
LATELY CHILD PSYCHIATRIST, WORKERS' SICK FUND, AND DIRECTOR OF THE MENTAL HEALTH CLINIC, ICHUD HAKIBUTZIM, ISRAEL

A PERSON'S childhood—his past—holds the clue to his present and his future. Forgotten or never consciously appreciated motives affect our actions and reactions more than the motives of which we are aware.

Nations, like individuals, have a past; and the national inheritance is handed down from each generation to the next, by command and prohibition and expectation. From the nation, as from his parents, each child absorbs associations, influences, and taboos which contribute more to his later character than those that are verbally expressed or consciously acknowledged.

The gigantic mythical canvases nations have painted for themselves are the adult's expression of a deep longing to identify with powerful, protective images, like those the child forms about his parents. The nation's past, with its heroic deeds and hardships and achievements, is the national joint origin of all its offspring; and, though it can be magnified to answer a need, it cannot be wholly invented.

THE PAST—JEWISH AND GERMAN

In trying to understand the Jewish past and its present significance, we have to look at the past of another nation, the Germans. For the association between them is long and peculiar.

The modified German language, Yiddish, is the one which the Jews adopted as their international tongue, and which still enables immigrants in Israel to understand each other when their native languages are different. Nor is this tie one-sided. There was no united German language till Luther's translation of the Bible.

For a people to take over the language of another means a very close association indeed. It implies a mutual dependence, an attraction, no matter how much of ambivalence, fear and hatred, contempt, or depreciation are mixed with it. Our love choice often attracts us to objects which our reason does not approve. The attraction of opposites, the highly emotional character of the Jews and the intense emotional confinement of the Germans, also played a part.

The other binding tie is the experience of the second world war and what preceded it in Germany. It is rare to find a European new immigrant in Israel whose family were not exterminated or put into camps by the Germans. Survivors of those camps form a substantial part of the population. If people stand vis-à-vis as persecutor and persecuted, each must absorb the mentality of the other. It is impossible to be human and not be affected by such experiences. Just as the persecutor acquires some doubts about the guilt of his victim, the persecuted begins to doubt his innocence.

While we can see that the Israel of today is profoundly affected by the Germany of yesterday, the question remains—what caused this eruption? And it is here that the past emotional experiences and the resulting characters of the two nations give a clue.

The German past has two outstanding features: first its ancient vandalism, which had so large a share in the destruction of the Roman Empire; and, secondly, the fact that Germany became a nation after all others. Taking the second point first, we may say that the Germans, in the national sense, had no real parents. They could look back only on centuries of uncertain allegiance, partial revolts, hostile acts with a large residue of guilt, and finally a coercion—literally—into adulthood and national unity. Lacking a settled framework, with both love and acceptable restraint, the development of Germany has corresponded to that of an orphan who has been much knocked about; and the behaviour of the Germans has in fact been very much what we see in such unfortunates. In the past sixty years they have alternated between periods of strenuous painstaking effort and periods of unbridled aggression, when all previous standards were overthrown. At one time their behaviour has resembled the attempt to placate a stern demanding foster-parent; at others there have been outbursts like those of a child unable to contain his hate and resentment.

If we think of Germany as lacking both emotional security and a rational adjustment to reality, because of the lack of a joint, heroic, satisfying past, we must also recognise a longing for such security. This longing to be approved and loved explains the positive efforts made to that end, just as its frustration explains the fury unleashed. Wagner, to fill the national want, endeavoured to produce a glorious saga of the German past, but succeeded only in creating immortal music. Neither man nor nation can acquire parents quite other than those they had.

The Jewish past is altogether different. Not only did the Jews become a nation early but their nationhood was expressed in an unusually exalted way. Rulers or kings commonly descend from gods; but for a whole nation to be chosen by God must reflect a widespread longing for identification with a father figure—omnipotent, omniscient—of an intensity which is quite exceptional. That this sense of being chosen grew stronger through the generations, and that the voices of reprimand were attended to, is evidence of its appealing to the masses sufficiently to answer their need. The punishing, demanding, aspect of this Jewish God has struck Christian observers as prehistoric and savage; but the price of protection by so powerful a father is behaviour suited to such a high ideal.

The paradoxical situation of the Jews during the last 2000 years becomes more intelligible if one notes that throughout the Old Testament objective truth always takes second place to the subjective: yet normally one sees the faults of others before (if at all) one's own. In the same way, the Jews, when they became exposed and helpless minorities, went on proclaiming their superiority—insisting that they must not be mixed or absorbed. Not only did this run contrary to the normal human tendency to adapt for survival but it inevitably led to their becoming a target for attack. In a setting where external reality was defenceless, internal reality claimed a uniquely protected position. To create for oneself such difficulties—to want to test out such a situation—the motivation must be instinctual and irrational.

What maintained it? The same longing which created this unique God remained active; and external reality was powerless against it, as it is against other ideas. Moreover the Bible shows that, just as there was continually the highest possible moral aspiration, there was an equally continual threat, and fact, of punishment for falling short. The God of the Jews appealed as much to the need for punishment as he demanded perfection in his

service. If the idea of having such a God could not be given up, neither could the idea of punishment be separated from it. The national inheritance found expression in exaltation at one end of the scale and in fear of being unworthy—of needing punishment—at the other.

In the situation of the Jews throughout these centuries we have an example of how human ambivalence works: how hope and fear create corresponding conditions in which they become external reality and present justification—evidence for the very emotions that called them to life. These extremes, equally strengthened, continue to act as forces of Nature do, by impetus and inertia. An individual is powerless to reverse the process, because the link that binds him has been fashioned in his childhood.

The Jewish God was no fickle parent, unpredictable and changing, but one giving exaltation and handing out punishment with a mighty, unerring hand. The Germans, on the other hand, had no united secure father-image, but a longing for the emotional security that a historic past provides. The mutual attraction of people with such different backgrounds can be understood psychologically. Thus, though every nation has at times filled the role of persecutor to the Jews, none ever reached the frenzied hatred the Germans have shown. The excessive German nationalism—another attempt at reshaping the past and the present—was in its midst confronted by a people, helplessly exposed, who yet seemed to have just that cherished possession. In the irrational attempt to wrench it from them, their combination of challenge and inability to hit back roused, and then appeared to justify, any and every brutality. Like all emotional outbursts, this led to a strengthening of its component factors; it increased the insecurity of the Germans and the guilt feelings of the Jews.

In the Jewish situation the new element, now increasing in importance, is the creation of Israel. It is as though the specific need for exaltation and punishment has exhausted itself in its existing form and can now be modified sufficiently to fit other conditions. But, though country and mode of life have altered, the ancient inherited ambivalence—the national character—is the same. It explains the Israel of today more truly than any survey of external conditions could possibly do.

ISRAEL'S PRESENT

In one way, Israel stands in the same relation to Europe as the latter to America. In the United States, dialect, custom, scenery, and culture change within thousands of miles—in Europe within hundreds. In Israel such change occurs within visible distances. The small size of the country, and the fact that it contains people from 70 nations, mean that the human groups must be small; yet they bear all the characteristics of their origin. Though one expects diversity, one is astonished by the presence of every feature of other countries, and all pronounced.

Even the diversity of the scenery seems to promote extremes of human response. The Dead Sea, the deepest land point in the world, looks like a symbolical expression of the depth Nature may go to. Then there is the desert, with its enmity to life which only great vigour can subdue. Yet one can conceive nothing more bountiful than a laden orange grove, or the trees bursting into flower so urgently that leaves appear only as an afterthought. The barren and the fruitful exist side by side; and just as the one holds out evidence of rich reward, the other reinforces the ever-present anxiety that devastation may win the day.

This hope and fear are part of the universal human inheritance—the response to the two facets of Nature. But their degree depends not only on inheritance but on personal experience and on the ways in which the prevailing culture requires and permits their expression. When we think of the different origins, experiences, and cultures of the new Israelis we find their variety much less surprising than their similarity.

To understand this similarity we have to turn back and consider what they had in common in the past. They had an idea which they shared, that of their God—an idea which has isolated them to some extent from the people they lived with, and has made them into a minority. The inborn ambivalence of hope and fear has found external conditions in which it was strengthened. The hope was attached to this personal God, at once so mighty, so impersonal; the fear to the actual and potential suffering from their minority status. To have survived at all is equivalent to the hoped-for miracle, but the conditions of this survival gave ample proof of punishment, and it aroused guilt.

The hope and fear remain intense in Israel today. But the object to which they are attached is no longer quite as abstract as God: it is their new country.

The hope—the conviction—that objective obstacles, no matter how great, can be conquered has expressed itself again and again. There is truth in the humorous saying that those who do not believe in miracles, in Israel, are no realists.

When on successive visits I saw the growth and expansion of every effort, I could not understand at first why the corresponding contentment and confidence were lacking. Nowhere are people so ready to exclaim: "It could only have happened here"—meaning this negatively, belittlingly, doubtfully. Moreover the greater an Israeli's own effort and sacrifice, the greater seems his readiness to blame and criticise. But later I recognised that when external reality is approached with an overwhelming emotional drive, objective success cannot be used as evidence of fulfilment. The drive goes far beyond what can be achieved, and will therefore be dissatisfied with whatever is created. At this point doubt and anxiety take the place of confidence, and find justification for self-reproach. In the Jews, moreover, experience of abnormal criticism and contempt, not to speak of persecution, have bred associations and fears which must again be externalised.

This ambivalence in regulations, business, and formal education robs the "yes" and the "no" of effectiveness, but by making them into continued irritants recreates the ambivalence.

There are two enterprises, however, in which the desire to succeed has been almost absolute, and therefore the ambivalence has been banished. Because they are plainly necessary to the survival of Israel as a Jewish National State, both have been tackled with an efficiency which comes from single-mindedness; and neither attracts the criticism or doubt associated with other national or individual activities.

One of these is the training and maintenance of the army, and the other is immigration. Agreement about these needs overrides almost every other difference, so that their truly great demands are accepted and their fulfilment is contemplated with pride and contentment.

As always when people depart from a neurotic pattern, and tackle their situation more rationally, the results are therapeutic in themselves. The value of the Israeli army in moulding its diverse human material into a homogeneous shape cannot be overestimated. Arrivals from Africa, Asia, Europe, and other continents, different in so many ways, are put through an intense, equal, and indiscriminate training—almost like mixtures of iron ore to make steel. Nor is this training wholly military; for these young people often do the greater part of their service in groups sent to agricultural settlements where they assist with civilian tasks while remaining under strict discipline. The composition of these groups—how many *sabras* or natives, how many new immigrants, what types—seems to be designed to strengthen their integrating, binding influence. I know of no other country where rejection by the army is generally regarded as an almost unbearable disgrace.

As for immigration, the number of refugees who came to Britain after the Hungarian revolution would be accepted in Israel without difficulty in a few weeks, though they might come from many different parts of the world. The flexibility and efficiency with which immigrants are absorbed is understandable when one realises that this absorption is one of *the* purposes, the devoted tasks, of this country. Solution of its problems—organisation, reception, finding homes, arranging Hebrew language courses—thus becomes a matter of course.

The fact that the national revival of the Jews is on an international basis has made its aims exceptionally difficult to realise; but it is succeeding. In the transmutation of a common God to a common country, an idea taken from one realm has been adapted to another. The world today contains many different cultures which find it hard to tolerate each other; yet, in the proximity enforced by narrow geographical boundaries, people from all these cultures are resolving their differences instead of magnifying them. They are doing this because of the supremacy of a common idea; and their success illustrates once more the fact that quite different kinds of people can be brought to live together.

Despite friction, discontent, difficulties of every sort, Israel is an accomplished fact, proving that unity on essentials is possible. As so often elsewhere, the finding of an outlet for an emotional, irrational craving has led to a more rational, better integrated existence.

(*To be concluded*)

Dialogues of Today

THE FINAL WEAPON

APOLLODORUS: Welcome Socrates! Where have you been? You look depressed and worried.

SOCRATES: I am not depressed, Apollodorus, but I am certainly worried, for I have just been listening to a debate in the upper house of the Assembly, where the leaders of the people have been discussing what should be done about the final weapon.

APOLLODORUS: Tell us, Socrates, what was said in the debate.

SOCRATES: There were two parties. Some said that we ought to give up the final weapon, as an example to others; and their opponents maintained that if we kept it, it would be less likely to be used.

APOLLODORUS: I should have voted with the first group, Socrates, for evidently things are going from bad to worse, and the building up of stocks of even more powerful weapons has done nothing to relax the tension, but has rather increased it. Besides, there seems to me to be a terrible fallacy in the argument that our possession of the final weapon is a guarantee of peace. That may hold good as long as neither side is sure that it could win a war without itself suffering serious injury. But one side has only to discover a new method of preventing its opponents' weapon from reaching it and it has the world at its mercy. And if we have staked everything on our armaments why should we expect mercy if our opponents beat us with the weapons we have chosen?

GLAUCO: I call that defeatism, Socrates, and if that policy had been adopted after the last war Athens would have been overrun by Sparta long ago. It is only our possession of the final weapon that has maintained peace so far. As for giving it up now, that would so dismay our allies and disturb the balance between our opponents and ourselves that it might well precipitate war. I believe that time is on our side. If we have strong nerves, and are patient, a time will come when we shall be able to negotiate with our opponents from strength, which is all that they respect.

SOCRATES: There is a story that a man once brought up a tiger, which he got as a cub, and which he trained to carry him on its back at the circus. One day when he was riding it, the animal, frightened perhaps by the cries of the crowd, appeared to go mad. And some spectators shouted to the man to get off, for if he stayed on its back it would inevitably kill him; but others told him to stay there, and do his best to control it, for, they said, if he got off, he would be in its power, and he was at any rate alive and unharmed so far.

APOLLODORUS: And which did he do?

SOCRATES: He did not get off, neither did he leave matters to chance; but, the story goes, Athene, who happened to be watching the circus, threw him a magic drug, which he gave to the tiger, and it became calm again, and did his bidding.

APOLLODORUS: I suspect, Socrates, that that is a parable, and that the tiger represents the final weapon.

GLAUCO: I think it stands for our opponents.

SOCRATES: Parables have more than one meaning. The tiger is the final weapon, but it is also the heart of man, which his reason strives to control. Each man has the responsibility for his own heart only, for he has no direct control over his opponent's.

ERYXIMACHUS: Parables are all very well, Socrates, but what would you do if you were the leader of the people? What is your magic drug?

SOCRATES: The magic drug, Eryximachus, is wisdom, the only gift Athene can bestow; and if you had it you would not need to ask what it is. As for me, I believe that the beginning of wisdom is to recognise one's ignorance, which is why I am always asking questions. But I will tell you what I would do. I do not believe that fear and mistrust can be dispelled by weapons, nor on the other hand that throwing them away will necessarily bring peace. If we cannot get rid of weapons because we do not trust each other, and if we cannot trust each other because we possess them, we must surely try to cooperate in some other sphere. So if I were the leader of the people, I would ask both our allies and Sparta to join with Athens in contributing part of what they spend on weapons to a common fund. And from that fund I would lend money to backward countries, so that they could build dams and make goods and improve the condition of their people, using their loans for these purposes to trade with the countries lending them the money. And I would use the fund, too, for research into health, and agriculture, and population control, and for educating backward peoples in these subjects. And so it would be seen by such peoples that they owed these benefits not to one or other of rival groups of nations, but to all working together. And if that happened I should no longer worry about the final weapon.

Special Articles

DISSEMINATION OF STAPHYLOCOCCUS AUREUS FROM WOOLLEN BLANKETS

K. F. ANDERSON
M.D. Lond.

R. A. W. SHEPPARD
B.Sc. Adelaide

From the Division of Bacteriology, Institute of Medical and Veterinary Science, Adelaide, South Australia

THE danger of hospital dust as a source of pathogenic streptococci has been repeatedly emphasised (White 1936, Cruikshank 1938, Hare 1941, Thomas 1941). Other organisms which have been detected in dust include the tubercle bacillus (Pressman 1937) and the diphtheria bacillus (Crosbie and Wright 1941). In hospital wards a large amount of dust is derived from blankets; and, although bacteria-laden particles settle rapidly to the floor, they rise again in a cloud when disturbed by draughts and sweeping (Wilson and Miles 1946). This view is supported by the work of van den Ende et al. (1940), who controlled airborne bacteria by the oiling of floors. van den Ende and Thomas (1941) later introduced oil-in-water emulsions for the treatment of blankets, and Wright et al. (1944) showed that the combined treatment of floors and of blankets substantially reduced cross-infection rates.

Pressley (1958), in a study of the fibre composition of hospital dust, has shown that samples taken at bed level consisted essentially of cellulose fibres; very few wool fibres could be found. Since most of the cellulose fibres contained *Staphylococcus aureus*, Pressley concluded that blanket fluff was not primarily implicated in the spread of *Staph. aureus* in hospital wards, and that the replacement of wool by other fibres which can be sterilised, or its treatment by oiling, is unlikely to reduce cross-infection.

Pathogenic staphylococci have always been isolated in this laboratory from woollen blankets whenever hospital outbreaks of staphylococcal infection have been investigated, and such blankets have been thought to play an important part in the spread of infection. Apart from the transfer of organisms by direct contact, either to the patient or to the nurse, the release of clouds of fluff during bed-making is probably an important mechanism in the transfer of infection to other bedlinen and to the anterior nares of staff and patients. The experiments recorded here were designed to demonstrate the dissemination of pathogenic staphylococci from an infected woollen blanket.

Similar experiments were not carried out in a hospital ward for two reasons. Firstly, the widespread occurrence of numerous phage-types of staphylococci would have made it extremely difficult to determine with certainty the source of any one colony isolated on the sampling-plates. Secondly, the introduction of an infected blanket into a general ward seemed an unjustifiable risk both to staff and to patients. A non-pathogenic marker organism was rejected on the ground that its behaviour might differ from that of a pathogenic staphylococcus. While these experiments are open to the criticism that they were not carried out under truly clinical conditions, they were designed to approximate as closely as possible to such conditions.

Materials and Methods

A new 100% wool blanket measuring about 80 × 60 in. was examined by the sweep-plate method of Blowers and Wallace (1955) to exclude the presence of pathogenic staphylococci. The blanket was then infected with a six-hour broth-culture of *Staph. aureus*, phage-type 80/81, using a wooden swab-stick which was lightly drawn across the blanket. No attempt was made to infect the whole surface, and small areas were chosen at random. The blanket was then hung up and allowed to remain at room-temperature overnight.

Experiment 1: Dissemination by Precipitation

The experiment was carried out in an empty room, measuring 24 × 36 ft., which had never been used as a hospital ward. A 5 c.ft. air sample was taken with a slit-sampler (Casella, London) to exclude the presence of coagulase-positive staphylococci. An area corresponding to the outline of the blanket was marked out on the floor, and culture-plates containing mannitol phenol-red agar were placed in position at floor level (fig. 1). The infected blanket was unfolded over the marked area by operators wearing masks, caps, and gowns, and was shaken gently at waist height and folded together, as in bed-making. It was then removed and was not allowed to come into contact with the floor at any stage of the experiment. The culture-plates were exposed, and fifteen-minute precipitation samples were collected.

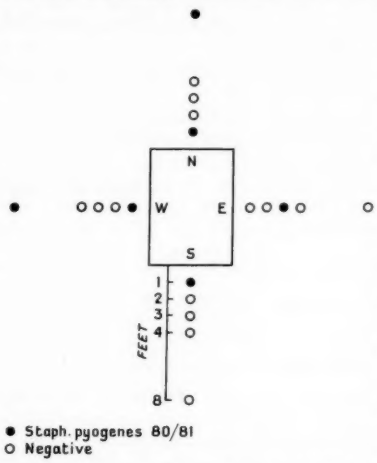


Fig. 1—Location of culture-plates in relation to blanket in experiment 1.

Experiment 2: Dissemination by Sweeping

At the end of experiment 1, the plates were removed and four new plates were placed in position 8 ft. from the marked area, which was then gently swept with a new broom in all directions. Precipitation samples were again collected over a fifteen-minute period.

Experiment 3: Dissemination at Bed Level

Four plates were placed in position at bed-level (29 in.), at a distance of 4 ft. from the marked area (fig. 2). The blanket was exposed and shaken as before, and fifteen-minute samples were collected.

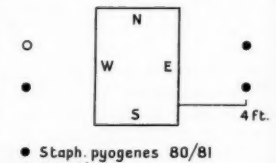


Fig. 2—Location of culture-plates in relation to blanket in experiment 2.

Results

Staph. aureus, phage-type 80/81, was isolated from four plates exposed during experiment 1. Three of the plates were 1 ft. from the marked area, and one was 3 ft. from it. After sweeping, two out of four plates showed the test organism at a distance of 8 ft. from the marked area.

Of the four plates exposed at bed-level, three yielded colonies of the test organism. In many of the plates

examined, the colonies had clearly developed in association with deposited fibres (fig. 3). Other colonies, which did not show fibres on superficial examination, were found to contain fibres when picked off and emulsified in saline solution for the coagulase test. Cellulose-acetate preparations of the fibres illustrated in fig. 3 were examined microscopically and showed the characteristic cuticular scale pattern of wool. The infected blanket was stored at room-temperature for two weeks after these experiments had been completed. At the end of this period colonies of the test staphylococcus could still be recovered by the sweep-plate technique.

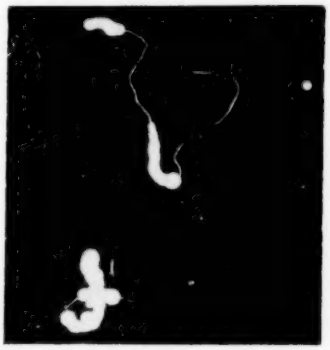


Fig. 3—Colonies of test staphylococcus associated with deposited fibres.

Discussion

These experiments confirm what is known of the general properties of blanket dust. This dust falls rapidly to the ground and is readily disseminated by sweeping. Infected fibres can be detected at bed height, 4 ft. from a shaken blanket—which is the average distance between hospital beds. Nurses commonly stand between beds when folding linen; so in practice infected fibres probably have only half this distance to travel in order to contaminate adjacent sheets and blankets. Experiments carried out to investigate the role of blankets in cross-infection must be specifically related to bed-making, and sampling methods must be used which will detect rapidly falling fibres in the vicinity of disturbed blankets. Samples taken at times unrelated to bed-making, or at some distance from the bed-making area and above bed-level, may fail to detect infected fibres originating from blankets.

We do not suggest that woollen blankets are solely incriminated in hospital cross-infection or that other fibres will not give rise to infected dust. Accounts of outbreaks of staphylococcal infection show that in some instances the nasal carrier is to blame (Penikett et al. 1958), while other investigators have demonstrated the importance of dissemination from the skin and clothing (Hare and Ridley 1958). Forfar and Maccabe (1958) declare that prophylactic measures should include the control of airborne infection resulting from the contamination of the atmosphere by dust from personal clothing, bedding, and fomites and the avoidance of contact with contaminated bedding. Probably all these factors play some part in staphylococcal cross-infection. The infected hospital blanket, of whatever material, cannot be excluded from the vigorous measures which must be taken to reduce the number of pathogenic staphylococci in general wards and maternity units.

Summary

In experiments designed to demonstrate the dissemination of *Staph. aureus* from an infected blanket, the survival of staphylococci on wool fibres for at least two weeks was confirmed.

Hospital blankets should be included in measures to reduce the number of pathogenic staphylococci in hospital wards.

Our thanks are due to the photographic department, Children's Hospital, Adelaide, for fig. 3, and to Mr. W. Nolan for figs. 1 and 2.

REFERENCES

Blowers, R., Wallace, A. T. (1955) *Lancet*, i, 1250.
Crosbie, W. E., Wright, H. D. (1941) *ibid.* p. 656.
Cruikshank, R. (1938) see *ibid.* p. 841.
Forfar, J. O., Maccabe, A. F. (1958) *Brit. med. J.* i, 76.
Hare, R., Ridley, M. (1958) *ibid.* p. 69.
— (1941) *Lancet*, i, 85.
Penikett, E. J. K., Knox, R., Liddell, J. (1958) *Brit. med. J.* i, 812.
Pressley, T. A. (1958) *Lancet*, ii, 712.
Pressman, R. (1937) *Amer. Rev. Tuberc.* **35**, 815.
Thomas, J. C. (1941) *Lancet*, i, 433.
White, E. (1936) *ibid.* p. 941.
Wilson, G. S., Miles, A. A. (1946) Topley and Wilson's Principles of Bacteriology and Immunity; vol. 2, p. 2005.
van den Ende, M., Lush, D., Edward, D. G. ff. (1940) *Lancet*, ii, 133.
— Thomas, J. C. (1941) *ibid.* p. 755.
Wright, J., Cruickshank, R., Gunn, W. (1944) *Brit. med. J.* i, 611.

Public Health

Soft Drinks

A REPORT by the Food Standards Committee, published on Feb. 25, examines the need for control over the composition, labelling, and advertising of soft drinks and contains proposals for revision of the Food Standards (Soft Drinks) Order, 1953.

The committee consider that the wide variety of soft drinks and the lack of information about their composition may give rise to confusion. Where soft drinks contain fruit constituents, they recommend that, for the guidance of purchasers, manufacturers should be required to declare on the labels the amount of fruit or fruit juice which the drinks contain. They take the view that soft drinks should be sweetened wholly with sugar or other carbohydrate sweetening matter and that the use of saccharin or other artificial sweetening agents should be prohibited, but that apart from this statutory control over the composition of carbonated and flavoured beverages is not necessary.

In the opinion of the committee no soft drink, whether sweetened with sugar or with glucose, is a sufficient source of carbohydrate to justify claims of energy value. They propose therefore that the use of any form of testimonial or nutritional claim based on the carbohydrate content should be prohibited in labelling and advertising. They also recommend that a special standard for glucose beverages is not justified and that use of the term " glucose " should not be permitted in labelling and advertising soft drinks.

Hygiene in the Dairy

The new Milk and Dairies (General) Regulations, 1959, which come into force on March 8, include provisions requiring workers to wear clean and washable overalls and head covering when milking cows or handling milk in open containers, to cover open cuts and abrasions with a waterproof dressing, and to refrain from spitting and smoking. A local authority is also given power to pay compensation to a worker who sustains damage or loss through being debarred by the medical officer of health from employment connected with milk, including the milking of cows, because he is suffering, or has been in contact with a person who is suffering, from a disease liable to cause infection of milk.

Influenza

In England and Wales deaths from influenza in the week ended Feb. 21 totalled 1121, 952 of these being of patients aged 55 or over. This mortality level is less than half that of the peak of the 1951 outbreak, and is similar to the levels in the winter of 1953 and the autumn of 1957. The peak of the present outbreak has now apparently been passed. Deaths from pneumonia and bronchitis also increased in the week ended Feb. 21. New claims to sickness benefit increased by 108,809.

In England Now

A Running Commentary by Peripatetic Correspondents

FOR the second time in my life my chins outnumber my teeth, and my medical adviser, who is clever and can read E.C.G.s, prescribed a driver to drive me round my practice. Advertisements produced lots of recruits, mostly from my more irresponsible patients, who wouldn't be allowed to drive bumper-cars at a fairground. One youth claimed that he purposely had no driving-licence so that it couldn't be endorsed. His friend, who believed in doing things in style, actually had a licence, but must have got his blood-group mixed up with his application form, because he was entitled to drive only an obscure group of agricultural contraptions. I can recommend him to any G.P. wishing to do his rounds on a combine harvester.

I worked through the applicants on the short list, and next day found myself progressing, like an epileptic grasshopper attempting the cha-cha, at the mercy of a lady who assaulted fiercely every pedal and knob she could reach. It reminded me of an octopus playing a cinema-organ and ended dramatically when she jerked the cigar-lighter (red-hot) up her sleeve.

Under her successor, a morose man, we began like the Ancient Mariner's ship, " Backwards and forwards half her length, With a short uneasy motion ", before grinding solemnly into a horde of oncoming traffic. Its direction and density were not due, as my driver suggested, to the crowds leaving a football match, but to our going wrong way down a one-way street. He was also incorrect in believing that he had been driving for so long that everybody should know he always put out his right trafficator when turning left.

My next recruit was a muscular female who wrestled the wheel as though it was a steer in a rodeo. Cornering, I could have leaned out and picked up a handkerchief with my teeth. Actually, I stayed inside and picked up my teeth with my handkerchief. Never did this driver's passengers start or finish their journey at the same time as the car. They all assembled on the back seat at the start and the front seat at the terminus, the majority in an attitude which suggested that they were about to be cut for the stone. I usually emerged from the car as though fired from an ejector-seat and " fell to earth I knew not where ", amidst the interested cries of the patients towards whose house I had been projected.

My last candidate was so myopic that her correction should have been built into the windscreen. En route for my house, she was discovered on the main runway at the local airport, complaining about these big lorries rushing at her along the crown of the road with both their trafficators out at once.

My latest E.C.G. looks like a Kew seismographic recording of a major earthquake whose epicentre is next door but one, and my medical adviser, who is clever and can read E.C.G.s, says I should be better off with a push-bike.

* * *

We already have many potent anabolic androgens, to say nothing of a chain-gang of long-acting testosterone esters, each with a different number of links in his chain. The trouble about the steroid nucleus is that it has a never-ending series of permutations and combinations—a halogen here, a hydroxyl or a keto there, and oh, those double bonds! Within the next five years I, for one, will certainly be a crazy, mixed-up steroid student.

* * *

We are disappointed that your correspondent, in his informative report of the yenwupongine congress (Feb. 28, p. 467) omitted any mention of what many of us considered the most important paper. This was the brilliant and provocative account, supported statistically, by Bacon et al. of the effect of half-hourly intrathecal infusions of baked yenwupongine in Muscovite turkeys. These injections completely reversed the usual 5-H.T. (serotonin) patterns, but the most surprising and significant change was seen clinically. When these birds were placed in the oven and cooked in the usual way (regulo mark 4·355), an explosion occurred after 9 hours. What was then seen, in Bacon's own words, " had to be seen to be believed ", for when the oven doors were opened and the smoke had cleared, it was seen that each turkey had become a phœnix. Further work on these findings is urgently needed, but we feel, though Bacon himself is being cautious in his claims, that he and his colleague are probably on the verge of solving the mystery of the dark lady of Shakespeare's sonnets.

* * *

There is a future for portmanteau words, and I hereby launch one. I told my wife I was going to the headquarters of our regional board. " Oh," she said, " are you going to a commeeting? "

Any consultant to his wife:

" Trip no further, pretty sweeting,
Journeys end in a commeeting."

* * *

When we first came to Queensland our children declared that nothing would make up for the lack of tobogganing and skating; but they have come to appreciate Christmas holidays on " the coast " (not " the seaside ").

The ocean can be very calm, but often from a hill one sees long lines of white rollers dividing a dark blue sea from a curve of hot white sand, flanked by the dark green scrub. Few things are more exhilarating than to spend an hour or two in this surf, and few sensations more exciting than shooting down the front of a wave 4–6 feet high, and then feeling it break just behind you. The foam roars in your ears as at first you surge towards the beach, and finally the whole length of your body glides gently on to the sand.

On our first holiday we hired an outboard motor boat to explore one of the coastal rivers. The estuary gradually narrowed and the mangrove swamps were exchanged for tropical rain forest with a great variety of trees, including palms and vines. The cicadas produced an incessant high-pitched chorus and there were many pelicans, parrots, and other birds. Apart from occasional sugar plantations the river was doubtless much the same as when Captain Cook sailed past its mouth on his way to the Barrier Reef.

* * *

Why did my school pay no attention to Greek? The other day someone sent me a report of a conference on " Ataractic and Hallucinogenic Drugs ". A search of an atlas showed no traces of a country called Ataraxia so I shook the moths out of my elderly *Materia Medica* and searched there with no better success. Finally the *Oxford Dictionary* told me it meant " without disturbance " and indicated a mood of stoic indifference. This shows how far we have advanced. The stoics needed long periods of privation and exertion, with foxes gnawing at various parts of their anatomy, before they could achieve this stern mood. Now it is to be had on demand at the nearest surgery for the modest fee of a shilling.

For those who are research-minded a small fox may be installed in the waiting-room and the patients subjected to the bite-test at intervals.

* * *

SPRING AGAIN

When coughs and colds are all around
And Income Tax demands abound;
When coiled in bed with icy toes
You cannot bear to don your clothes;
Then is the time to rise and sing
A welcome to returning Spring.

Unhitch yourself from counterpane,
Pour bronchial mixtures down the drain,
Discuss no more insipid diet—
" Here's a beefsteak, woman, fry it! "
Gulp a glass of vintage brew.
Forget that you have had the 'flu.

Come forth into the sun and see
The green buds bursting on the tree,
The flowers bloom, the grasses blow,
A nesting bird in each hedgerow—
Busy as a bee or beaver—
Atishoo! O, my God, hay-fever!

Letters to the Editor

MENTAL HEALTH BILL

SIR,—Some of your correspondents welcome the administrative changes in mental hospitals which may result from the Mental Health Bill. Some would wish to cast these hospitals in the general-hospital mould and to model themselves on the pattern of their colleagues in general medicine and surgery. Others think the possible demise of the medical superintendent may give them greater freedom.

In the matter of equality with general hospitals let us remember, with the Swiss Constitution, that the principle of equality is violated when unlike things are treated alike, and that hospitals mainly devoted to the care and treatment of the mentally ill and subnormal will always be unlike general hospitals in many essential respects. Psychiatric patients treated in general hospitals are likely to be specially selected, and, in spite of modern techniques—or paradoxically because of them—an increasing proportion of patients in the other hospitals will take longer to cure or become chronic, and will need a carefully planned therapeutic environment for a long time. This, particularly in hospitals for the subnormal, can be maintained only if there is one individual, living within the community and sensitive to its atmosphere, who is responsible for its control. This is essentially a medical function and a matter for an individual and not a committee.

All medical superintendents, except perhaps a few remaining from the old school, will welcome the clinical freedom given by the Bill to "the responsible medical officer". Legal responsibility for patients under the clinical care of others of equal professional status has always been objectionable—but there seems to be no reason why the medical superintendent, as *primus inter pares*, should not continue to function as chief officer of the hospital and to order its affairs in consultation with his colleagues so that an atmosphere suitable for their work can be maintained. The alternatives seem to be succumbing to tripartite administration, which has been likened to "three men in a boat with nobody at the helm", or to lay control. Nobody would wish to belittle the excellent work of the well-trained and experienced lay administrator in his own field, but few would consider it proper to give him responsibility as "principal administrative officer", under H.M.C. (48) 2, for a type of administration which is essentially medical. In spite of the puzzlement of your correspondent "deputy physician superintendent" by the idea that the ordering of furniture is as essential as psychotherapy, is not the design of a chair as important to a feebleminded spastic as psychotherapy to a neurotic ?

Northgate and District Hospital,
Morpeth, Northumberland.

C. GUY MILLMAN
Medical Superintendent.

INTERNATIONAL CERTIFICATES OF VACCINATION

SIR,—In the course of my duties a large number of international certificates of vaccination against smallpox are submitted to me. It is very clear that many doctors are unaware of the importance of these as essential documents for travel purposes, if one may judge by the inaccurate way in which they are completed. It is not uncommon to find that, though an international certificate has been asked for, the individual is supplied with a certificate written on the doctor's notepaper, or indeed on a sheet of blank paper. Such a certificate is valueless for travel purposes.

May I quote a very recent example reported from one of our ships? There were no less than 95 invalid certificates issued by doctors in all parts of the country; many of these lacked the official "approved stamp", many were undated, others failed to indicate whether a primary vaccination or a revaccination had been done, and often no result was recorded. Accordingly, large numbers had to submit to revaccination on board before reaching their destination.

In many countries admission is granted only on production of a valid vaccination certificate, and this is looked upon abroad as a legal document whose correctness is no less important than that of passengers' other immigration documents.

The certificate should show, when a primary vaccination has been done, whether the vaccination has been successful; and the doctor's signature should be authenticated by the local public-health authority and duly stamped by that authority. The correct method of dating is indicated in the notes set out on the certificate. Doctors unable to obtain international vaccination certificate forms from their local public-health authority can obtain these from main passenger offices or from the Ministry of Health.

P. & O. Steam Navigation Company,
122, Leadenhall Street,
London, E.C.3.

I. J. CORBETT
Medical Superintendent.

INGUINAL HERNIA REPAIR

SIR,—Mr. Marsden has done a great service in drawing attention, in his article last week, to the immense difficulties in assessing hernia repairs.

Since 1956 I have been engaged on a series of repairs using a new technique and have based my records on his set of rules. If these are followed, then, as he says, some conformity will eventually result.

With reference to any repair operation, I feel it is necessary to realise two points of paramount importance: (1) the securing of complete absence of tension from above or below on the posterior wall of the inguinal canal, no matter how it is reconstructed; and (2) the elimination of any lax peritoneum on the medial side of the sac deep to the transversalis fascia. Residual tension on the posterior wall or lax peritoneum left in situ are in my opinion very possible causes of an unexpected recurrence.

Peterborough. D. W. BRACEY.

THE REGISTRATION OF INGUINAL HERNIÆ

SIR,—In four Liverpool general hospitals, since 1951, the repair of every inguinal hernia in a male of 16 years or over has been registered. The scheme is still in operation, but Marsden [1] has reported on the first thousand repairs to reach the end of the chosen three-year follow-up. I may be mistaken, but I think I detect a note of disappointment and baffled surprise when he finds he is forced to admit that he does not possess the answer to the question, which is the best method of repairing an inguinal hernia. With commendable constancy of purpose he relegates the first thousand repairs registered to the role of a preliminary skirmish with the problem, stating confidently that a total of three thousand will be needed to solve it. I have an unpleasant feeling that, unless he is lucky, he will be even more disappointed and even more baffled after he has analysed the three thousand.

1. Marsden, A. J. *Brit. J. Surg.* 1958, **46**, 234.

Briefly, the reasons for my misgivings are:

1. Before me, as I write, I have the published reports of 21,643 repairs, the largest single series being 5525. In this mountain of clinical experience the solution to the problem remains buried, and I just wonder if tossing an extra 3000 on to it will do what the other thousands have failed to do.

2. The pattern of the Liverpool investigation, as published, is closely similar to those of Fallis,[2] Shelley,[3] and other American authors. The method has failed in the past, and I am wondering what has suddenly made it effective.

3. Faced with "statistical difficulties" [1] due to numerous intercurrent variables, science does not, as far as I am aware, proceed to open a register in order to circumvent them.

4. Theoretically, there is no reason why registration, as a method, should succeed because it is based on Baconian empiricism, which suggested that the solution to a problem would fall, automatically, like a ripe plum, from a mass of observations, provided that mass was sufficiently large. I think I am right in saying that no-one except Bacon ever believed this to be true, and modern scientists certainly do not.

The defects of Baconian empiricism cannot be overcome by the stricter attention to criteria which Mr. Marsden recommends in his article in your last issue. Some important variables may be unknown, and those that are known cannot be precisely defined.

Tutnall,
near Bromsgrove, Worcs. F. S. A. DORAN.

SEX REVERSAL IN NEWBORN BABIES

SIR,—The results described by Dr. Moore (Jan. 31) suggest that fertile XX males might be worth looking for particularly among fathers of 5 or more daughters but no sons (where $P < 5\%$).

Marine Biological Laboratory,
Woods Hole, Massachusetts, U.S.A. RALPH A. LEWIN.

ANASTOMOSIS IN THE CORONARY CIRCULATION

SIR,—In your issue of Jan. 24 Professor Blumgart and Dr. Zoll commented on our paper on Anastomosis in the Coronary Circulation.[5]

We consider that in our paper we gave adequate reasons for developing a more direct method of demonstrating coronary anastomoses than that devised by Schlesinger.[6] We would, however, like to take this opportunity to state that all the hearts studied by us were injected with a mass made from 'Analar' brand of lead acetate [7] and 'Judex' brand of anhydrous di-sodium phosphate [8] (or its equivalent measure of the hydrous salt). We found that the use of other well-known brands yielded particles of significantly smaller size. The use of gelatin as a suspending agent did not alter the penetration of particles through a Baird and Tatlock grade-3 filter when compared with an aqueous suspension of the same lead phosphate. Also, estimation of the calibre of the smallest vessel penetrated was made by an independent histopathologist.

Our "aberrant" results are possibly not as far out of keeping with the findings of other workers as they at first appear to be. The main difference of opinion seems to be whether anastomotic channels are formed as a result of disease or whether they exist in the majority of normal healthy hearts and allow of the patient's survival in the face of coronary occlusion. We believe that our findings suggest the latter to be the correct explanation, and that they agree with those of other workers: for example, Baroldi et al.[5] state that "The most important finding in normal hearts was the presence of numerous anastomotic vessels with a lumen varying between 50 and 350 micra."

2. Fallis, L. S. *Ann. Surg.* 1936, **104**, 403.
3. Shelley, H. J. *Arch. Surg.* 1940, **41**, 747.
4. Laurie, W., Woods, J. D. *Lancet*, 1958, ii, 812.
5. Schlesinger, M. J. *Amer. Heart J.* 1938, **33**, 420.
6. 'Analar' brand of lead phosphate made by British Drug Houses, Poole, England.
7. 'Judex' brand of di-sodium phosphate made by the General Chemical and Pharmaceutical Company Ltd., Sudbury, Wembley, England.
8. Baroldi, G., Mantero, O., Scomazzoni, G. *Circulation*, 1956, **4**, 223.

Prinzmetal et al.[9] [10] in a series of papers found that the "normal human heart has an extensive collateral circulation . . .", and, in one experiment using graded glass beads as a perfusing agent, demonstrated anastomotic channels 70–170 micra in diameter in eleven of thirteen healthy hearts obtained from patients whose ages ranged from 4 to 73 years.

Prinzmetal et al. suggested that the anastomotic vessels found in the hearts of patients with chronic ischæmic heart-disease were not new vessels but "merely enlarged or enlarging pre-existent vessels". With these views we agree, but note that in some instances these channels are absent both in healthy and in diseased hearts, possibly owing to inherited characteristics.

Perth, Western Australia. W. LAURIE.
Edmonton, Canada. J. D. WOODS.

DEATH OF A TESTICLE

SIR,—Dr. K. W. Lovel's conclusion last week, after his research into the correct use of the term gangrene—to wit, that gangrene should be defined as "tissue death with putrefaction"—is precisely that which my colleague, R. J. McNeill Love has taught for more than 30 years. This is the definition given in our textbook, and this is the definition I had in mind when I wrote my letter of Feb. 21.

It is this very definition that upholds what I had to say in that letter, for seeing that the coverings of the testis and the whole scrotum have a separate blood-supply, differing from that of the testis and its epididymis, how otherwise than by bacterial invasion and putrefaction could local death occasioned by torsion spread from the testis, through the tunica vaginalis and the coverings of the testis, to the scrotum?

Sholden, near Deal,
Kent. HAMILTON BAILEY.

SIR,—I am indebted to Mr. Hamilton Bailey (Feb. 21) for pointing out the absurdity of my statement that torsion of the testicle is *never* followed by gangrene. I hope that his letter was not intended to imply that gangrene *always* follows.

The clue to this apparent divergence of opinion lies in the presence or absence of infection. Mr. Bailey's cases were presumably infected either via the blood-stream or the vas deferens, and the extension of gangrene to the scrotum suggests that the infection was of a peculiarly virulent nature.

I have operated on a fair number of these cases, and agree that the testicle is both dead and discoloured. I also agree that orchidectomy is usually the best and quickest way to relieve the patient of his symptoms. Nevertheless, under extenuating circumstances comparable to those I described, conservative treatment is both logical and effective. I have little doubt that many cases, particularly in adults, have been so treated "by mistake".

Ischæmia alone does not produce gangrene, which is, by definition, a putrefactive process. There are so many examples of this basic truth that I did not think it necessary to labour the point. We are all familiar with the diverse effects of infarction in the heart, lung, brain, spleen, intestine, and limbs . . . and will have seen occasional cases where pulmonary infarction has been followed by infection, gangrene, and abscess formation. The quiet avascular necrosis associated with fractures of the femoral neck is in familiar contrast to the sequestration of bone which follows infective necrosis of the terminal phalanx of a finger.

Ligature of an aberrant renal artery is usually followed by aseptic infarction, but occasionally there is a stormy sequel

9. Prinzmetal, M., Simkin, B., Bergman, H. C., Kruger, H. E. *Amer. Heart J.* 1947, **33**, 420.
10. Prinzmetal, M., Bergman, H. C., Kruger, H. E., Schwartz, L., Simkin, B., Sobin, S. S. *ibid.* 1948, **35**, 689.

with torrential hæmaturia demanding secondary nephrectomy. A surgeon about to tie such a vessel might profitably ascertain whether the urine is infected before coming to his final decision.

I see no reason why the testicle should behave differently from any other organ or tissue . . . and I do not believe it does.

Barnet, Herts. V. J. DOWNIE.

VALLERGAN

SIR,—Dr. F. Widlake (Feb. 21) describes a complication of violent excitement which occurred in a child following the oral administration of a new sedative, trimeprazine tartrate (' Vallergan ').

During the use of this drug for premedication in some 500 cases at the Hospital for Sick Children, Great Ormond Street, I have never seen or been told of such unusual behaviour as Dr. Widlake describes. An article by Dr. W. J. Glover and myself which describes a trial of this drug in hospital is now awaiting publication in your journal. From this trial I can suggest that it seems just possible that Dr. Widlake's patient reacted so unexpectedly owing to the chosen dose being rather too small to produce efficient sedation, only producing excitement in the same way that a mischosen or mistimed dose of barbiturate occasionally does.

Vallergan appears to me to be a " better promethazine ", and if so then it would seem to be a very valuable premedicant drug for children.

University College Hospital, London, W.C.1. R. W. COPE.

THE CRANBROOK REPORT

SIR,—I refer to last week's letter from my very good friends Mr. Wrigley and Mr. Garland.

The admirably constituted Cranbrook Committee was appointed *by* the Minister, and, after thorough consideration of evidence from all relevant sources, recently reported *to* the Minister.

On the other hand, Mr. Wrigley is one of two advisers in obstetrics to the Minister; Mr. Garland is an active and capable member of our largest regional hospital board. This being so, I suggest that it might have been wiser or at least more appropriate for them also to present their opposing views to the Minister rather than to launch them upon a public of which the vast majority can be only very partially informed. None of the Cranbrook recommendations has as yet been implemented: there is plenty of time.

Unfortunately, and all too paradoxically, any discussion of the affairs of midwifery is apt to arouse the vilest passions; special pleading on behalf of sectional and parochial interests ad nauseam obscures a main issue which should be so happy in its outcome. Is it therefore too much to expect a measure of manifest agreement at the outset and at the centre? Whether we like it or not Savile Row *is* the administrative centre in this country. I only hope that it will at last prove itself worthy of the leadership entrusted to it (bearing in mind that leadership connotes a certain degree of discipline).

My object in addressing you, Sir, is not to take sides in the endless altercations as to who should deliver the baby and where the baby is to be delivered. Rather do I wish to call the attention of everyone concerned to the views expressed by Sir George Schuster and others in Creative Leadership in a State Service,[1] which I thoroughly endorse. Our maternity services at this juncture present a most important and serviceable illustration and a very great opportunity.

London, W.1. FRANK COOK.

SIR,—How refreshing it was to read the letter by Mr. Wrigley and Mr. Garland after the extreme disappointment evoked by the Cranbrook report, which brought to mind the epitaph of old Sir Hugh:

> ". . . In this case I confess
> Some reasons weigh more, and some weigh less.
> The case being so, we can hardly say no,
> And yet we hesitate, much, to say yes."

Surely the time has come to abandon the obvious inefficiency of tripartite control, and to unify the midwifery services under the vigilant eye of the obstetric hospital. This would bring every delivery indirectly under the guidance of the consultant.

Speaking as a future administrative doctor, I sincerely believe that the establishment of " local maternity liaison committees " would be a retrograde step, causing an even more Babel-like confusion where the single voice of authority is so clearly needed. And, speaking as a married woman, I think I can say that most of my sisters would be delighted to have hospital confinement, provided that they could be discharged within forty-eight hours. Only thus can we provide (and here I use the very words of the Royal College of Obstetricians and Gynæcologists) " maximum safety for mother and child."

London School of Hygiene and Tropical Medicine, W.C.1. VIVIAN G. EDWARDS.

ANTIBIOTICS AND THE COMMON COLD

SIR,—The common cold presents a very real problem in industry, to both employer and employee. It is a recurrent cause of interruption of planned production on the one hand, and of loss of earnings on the other. In one of our factories in December, 1958, 13% of the population each lost an average of seven days owing to upper respiratory infection.

Dr. Ritchie's carefully planned work and his accurate analysis of results [2] were most encouraging and led us, in this department, to look at the problem from a practical standpoint. We at once anticipated difficulties in carrying out specific antibiotic sensitivity tests annually on all our staff, even though we have a comprehensive bacteriological laboratory service. Professor Garrod (Jan. 3) raised once again the problem of inducing antibiotic-resistant strains as a result of minimal antibiotic therapy. To overcome these difficulties, and reduce by about $^6/_7$ the incidence of severe colds as was done by Ritchie, it seemed to us that the following conditions needed to be satisfied:

1. We must have an antibiotic to which a high proportion of the population showed sensitivity of their normal oronasal flora. Under this circumstance, swabbing of every individual would be unnecessary.

2. The possibility of creating resistant strains must be minimal and the consequences of such an occurrence negligible. An antibiotic which was insoluble and not absorbed, and therefore not used in systemic infections, would meet these requirements.

Our work was conducted in two factories. The first was a unit of 400 people approximately. We took nasal swabs from 120 people on a random basis and did antibiotic sensitivity tests. The results were as follows:

	Framycetin 50 µg. with gramicidin 0·5 µg.	*Chlortetracycline 100 µg.*	*Oxytetracycline 100 µg.*	*Tetracycline 100 µg.*
Sensitive in some degree ..	115	78	56	63
Antibiotic of choice * ..	104	11	1	1

4 cases were completely resistant.

* In some cases two of the antibiotics were equally effective and these have been included under two headings.

Thus 96% of the swabs were sensitive in some degree to framycetin (' Soframycin '), and in 86% of cases it was

1. Acton Society Trust. London, 1959. See *Lancet*, Feb. 14, 1959, p. 349.
2. Ritchie, J. M. *Lancet*, 1958, i, 615; *ibid.* p. 618; *ibid.* 1958, ii, 699.

the antibiotic of choice. On the basis of random sampling, the expected error of these two figures was $\pm 3^1/_2\%$ and $\pm 6^1/_2\%$ respectively.

We next considered the larger factory of some 2700 people, and took swabs from a random sample of these people. Sensitivity tests in 98 people gave the following results:

	Framycetin 50 µg. with gramicidin 0·5 µg.	*Chlortetracycline 100 µg.*	*Oxytetracycline 100 µg.*	*Tetracycline 100 µg.*
Sensitive in some degree ..	97	70	59	64
Antibiotic of choice * ..	94	17	9	12

1 case was completely resistant.

* In some cases two of the antibiotics were equally effective and these have been included under two headings.

Thus our first experience was repeated, and we deduced that if we applied framycetin in all cases of the common cold we could confidently expect this to be the right antibiotic in over 95% of cases. Furthermore, this antibiotic would not suffer the criticisms levelled at the other antibiotics which have been recommended for this purpose.

In a further group of 60 people, penicillin was included in the sensitivity tests. The results were:

	Framycetin 50 µg. with gramicidin 0·5 µg.	*Chlortetracycline 100 µg.*	*Oxytetracycline 100 µg.*	*Tetracycline 100 µg.*	*Penicillin 2·5* I.U.
Sensitive in some degree	56	36	23	28	27
Antibiotic of choice	35	1	1	2	20

2 cases were completely resistant; 1 case was sensitive only to penicillin.

These results would appear to confirm to some extent the opinions expressed by Professor Garrod and Dr. Wood (Jan. 31). Our figures indicate that just under 50% of cases were sensitive to penicillin; and that, when this was the case, in a high proportion of those sensitive penicillin was the antibiotic of choice. Nevertheless, on grounds of sensitivity, framycetin remained superior and had the other advantages already mentioned.

We have now embarked on a clinical assessment in which the standard treatment is 1 soframycin lozenge b.d. (each lozenge contains framycetin 10 mg. plus gramicidin 100 µg.) plus soframycin nebuliser b.d. for three days. It is hoped that results of this assessment will be available in three months.

The laboratory work in this investigation was carried out by Mr. R. M. Allison in the company's laboratory at Hayes, and we are indebted to Roussel Laboratories for supplies of 'Soframycin'.

T. Wall & Sons, Ltd.,
Atlas Road, London, N.W.10. PETER R. BATESON.

ORAL TREATMENT OF RINGWORM WITH GRISEOFULVIN

SIR,—Dr. Williams and his colleagues [1] described 9 cases of ringworm of the nails treated orally with griseofulvin. In connection with this I should like to describe the results of oral treatment with potassium iodide of ringworm of the scalp due to *Trichophyton violaceum*.

21 children aged 2–11 years recovered after being treated orally with a $2^1/_2\%$ solution of potassium iodide for 2–5 months. The doses ranged from 0·2 to 0·4 g. of potassium iodide, according to age, three times daily. Some of the children received also a local application of betanaphthol ointment or 3% tincture of iodine in an attempt to shorten the time of treatment. The usual precautions with administration of iodide were strictly observed. The complete recovery of the children was confirmed microscopically and by negative culture.

Further investigations are needed to discover the optimum dosage and the duration of treatment.

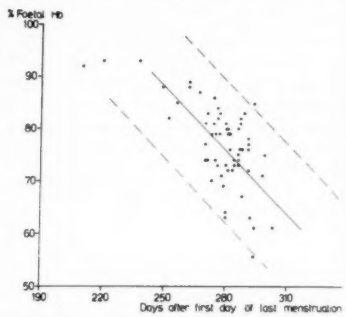
Tel-Aviv,
Israel. S. TULTCHINSKY-GOLDSTEIN.

1. Williams, D. I., Marten, R. H., Sarkany, I. *Lancet*, 1958, ii, 1212.

FŒTAL-TYPE HÆMOGLOBIN IN THE BLOOD OF THE NEWBORN

SIR,—Fœtal blood contains two different types of hæmoglobin (Hb)—fœtal and adult—which differ in the rate of alkali denaturation [1 2] and in several other respects.[2] The fœtal-Hb fraction gradually decreases during the latter half of the pregnancy.[3–5] The scatter of the fœtal-Hb values is considerable for newborn infants of approximately the same age.[5 6] Thus in my material [5] figures between 88 and 55% fœtal Hb of the total Hb were observed for infants at term (see figure).

The physiological significance of the level of the relative proportion of fœtal Hb in the blood of the newborn is unknown. In connection with a systematic study of the relative proportions of fœtal and adult Hb at birth I have made some observations which may throw some light on this problem.



Correlation between percentage of fœtal hæmoglobin and postmenstrual age. The interrupted lines are the 95% confidence limits (Brody [5]).

Blood samples obtained from the umbilical cord immediately after birth were analysed. The rate of alkali denaturation was determined spectrophotometrically, and the relative amounts of the different types of Hb were calculated according to the method of Betke.[2]

In five consecutive cases of severe neonatal jaundice (indirectly reacting bilirubin between 13·8 and 26·0 mg. per 100 ml.), determination of the relative proportion of fœtal Hb showed impressively high values—between 86 and 93%. Every known form of blood-group incompatibility is ruled out in these cases, and they apparently represent a type of exaggerated "physiological jaundice".

The experiments of Langley [7] indicate that the liver is the main site for the production of fœtal Hb, and that liver hæmatopoiesis is 3–5 times more intense in premature than in mature infants. On the basis of these findings it is logical to conclude that the intensity of liver hæmatopoiesis is inversely proportional to the degree of maturity of this organ. Furthermore, it seems conceivable that the relative proportion of fœtal Hb in the blood reflects the intensity of the hæmatopoiesis in the liver, and may therefore indicate the degree of maturity of the liver.

Neonatal jaundice not caused by blood-group incompatibility is considerably more common in premature than in mature infants. In most cases immaturity of the liver has been considered the cause, and recently it has been clearly demonstrated that deficiencies of liver glucuronosyl transferase [8–10] and uridine diphosphoglucose dehydrogenase [10] are essentially responsible for the increase of serum-bilirubin levels in the newborn. These enzyme systems are apparently formed during the latter part of the pregnancy.

1. Bischoff, H. *Z. exp. Med.* 1926, **48**, 472.
2. Betke, K. *Biochem. Z.* 1951, **322**, 186.
3. Beaven, G. H., Hoch, H., Holiday, E. R. *Biochem. J.* 1951, **49**, 374.
4. Zeisel, H. *Z. Kinderheilk.* 1951, **70**, 190.
5. Brody, S. *Acta obstet. gynec. scand.* 1958, **37**, 374.
6. Bancroft-Livingston, G., Neill, D. W. *J. Obstet. Gynæc. Brit. Emp.* 1958, **65**, 4.
7. Langley, F. A. *Arch. Dis. Childh.* 1951, **26**, 64.
8. Lathe, G. H., Walker, M. *Quart. J. exp. Physiol.* 1958, **43**, 257.
9. Grodsky, G. M., Carbone, J. V., Fanska, R. *Proc. Soc. exp. Biol., N.Y.* 1958, **97**, 291.
10. Brown, A. K., Zuelzer W. W., Burnett, H. *J. clin. Invest.* 1958, **37**, 332.

These facts make it seem likely that the maturation process of the fœtal liver proceeds, from a hæmatological point of view, in two distinct phases. During the first phase the liver is mainly concerned with the production of a special type of Hb that is particularly well suited for the intrauterine life of the fœtus.[2] During the second phase there is depression of this activity, and through the formation of certain enzyme systems the liver is being prepared for its function of conjugating and excreting the degradation products of Hb. It would seem that cessation of liver hæmatopoiesis is a prerequisite for the proper develcpment of this organ's bilirubin excretory capacity.

This preliminary report indicates that a very high relative proportion of fœtal Hb in the blood of the newborn, apparently signifying the persistence of intense hæmatopoiesis in the liver, is associated with excessive neonatal jaundice. This might imply that the determination of this Hb fraction at birth might be used as a measure of the degree of liver maturity in terms of this organ's capacity to excrete bilirubin. The correlation between the relative proportion and concentration of fœtal Hb and neonatal jaundice not caused by blood incompatibility, as well as other implications of this finding, will be published elsewhere.

Department of Women's Diseases,
Karolinska Sjukhuset, and
King Gustav V Research Institute,
Stockholm 60, Sweden. SAM BRODY.

GLUCAGON AND BODY GROWTH IN DWARF MICE

SIR,—In a previous paper on the relationship between the pancreatic islets and growth I concluded that pancreatic glucagon can stimulate body growth in pituitary dwarf mice.[1] Further data support this conclusion.

Hypopituitary dwarf mice of the Snell strain, 4 weeks old, were treated with glucagon or somatotrophin in standard conditions. In order to avoid the stress of repeated injections, the hormones were incorporated in cholesterol pellets and the pellets implanted under the dorsal skin once weekly.[2] Somatotrophin (Armour) or crystalline glucagon (Lilly, lot no. 258–234 B–54–2) were compressed in a pellet-making apparatus with cholesterol in order to obtain small pellets containing 100 μg. of either hormone; control cholesterol pellets were prepared without hormones. It was ascertained that a week after the implantation the pellet was completely absorbed. The results are summarised in the accompanying table.

EFFECT OF SOMATOTROPHIN AND GLUCAGON ON BODY-WEIGHT OF HYPOPITUITARY DWARF MICE

Duration of treatment (weeks)	Body-weight (g.) *		
	Control	Somatotrophin	Glucagon
0	5·305	5·221	5·215
1	5·261 (−0·8)	7·926 (+ 52·1)	8·303 (+ 59·2)
2	5·308 (+0·1)	11·908 (+128·5)	12·042 (+130·9)
3	5·471 (+3·2)	14·629 (+180·7)	14·010 (+169·8)
4	5·520 (+4·0%)	17·584 (+237·1)	17·834 (+242·0)

* Mean per cent. variation in parentheses.

From the table it appears that both somatotrophin and glucagon, at the given doses, stimulated the growth of pituitary dwarf mice to about the same extent. Moreover, in comparison with our previous results, it appears that glucagon and, especially, somatotrophin are more active when given in pellets than by injection; this could be due to the repeated stress of injections and/or slower and continuous absorption of the pellets.

Institute of Pathological Anatomy,
University of Pavia, Italy. CESARE CAVALLERO.

1. Cavallero, C. *Ciba Found. Coll. Endocrinl.* 1956, **9**, 266.
2. Ugrob, J. M., Lyons, W. R., Jordan, C. W., Jr., Li, C. H. *Endocrinology*, 1957, **61**, 477.

STAPHYLOCOCCI IN HOSPITALS

SIR,—Dr. Avery Jones (Jan. 24, Feb. 14) has drawn attention to the dirty state of the walls in many hospitals. The problem is especially difficult in the East End of London, since many steam trains traverse the district. The conditions are yet worse after many foggy days, and especially so when influenza incapacitates the wardmaids and porters.

At Bethnal Green Hospital washing of the walls of the eighteen wards and some of the other offices costs £1500. Even if the money were available (which it is not) to repeat the washing down, the problem would not be solved since the walls so soon get dirty. Washing the walls as far as the maids can reach is no solution and only draws attention to the grime. In the past year we have tried a different method.

A short-handled mop impregnated with an oily solution has been used for all the ordinary dusting of the ward furniture; this adsorbs the dust and does not spread it around. A similar mop fixed to a long bamboo cane is now being used to wipe down the walls once a week. It is light and easily wielded by the wardmaid, and the tops of the walls can be reached. By this method, a recently painted or washed wall can be kept clean, but it is not possible to remove the ingrained dirt from a wall which has not been painted for many years. The walls of the long corridor are also wiped down once a week by a porter, and the mop becomes so dirty that it has to be washed at once and reimpregnafed. At the present time the corridor walls are very dirty as a result of the fogs and illness among the porters, but most of the grime will be removed when the influenza epidemic is over. The walls of the ward in which this method was first used were painted in 1956 and washed down in 1957; they are still clean, and the wardmaid takes pride in her work. Great credit is due to the matron, the ward sisters, the domestic supervisor, and the hospital secretary in this attempt to keep clean the walls of a hospital situated in a very dirty area.

GEORGE GRAHAM
Chairman, Central Group
Hospital Management Committee.
London, E.2.

PHENACETIN NEPHROPATHY

SIR,—I am surprised that Dr. J. C. Eaton (Jan. 24) should express himself so strongly on the relative frequency of methæmoglobin and sulphæmoglobin when contradicting the statement in your annotation of Jan. 10 that methæmoglobinæmia is often the first sign of phenacetin intoxication.

So far as I know, certain differences between his results and my own while I worked in the Department of Medicine at Glasgow Royal Infirmary, although discussed, have never been satisfactorily resolved. In contrast to Dr. Eaton's observations I found in a smaller series of cases that, following the ingestion of both phenacetin and dapsone, methæmoglobinæmia is much commoner than sulphæmoglobinæmia, and that sulphæmoglobinæmia is rare without concomitant methæmoglobinæmia. Thus, in 20 patients with cyanosis suspected of being due to phenacetin, I found methæmoglobinæmia in 16 and sulphæmoglobinæmia in 4: in no case did sulphæmoglobin occur alone. In 45 tests on 19 patients treated with dapsone [1 2] I found methæmoglobin 36 times and sulphæmoglobin 5 times: in only 2 cases did sulphæmoglobin occur without methæmoglobin. Under the circumstances, and especially in view of Dr. Eaton's observations on routine blood samples sent to his department, I feel that even the brief report he gave should be accompanied by some reference to the methods used. Equally important is some indication of the anticoagulant used, the conditions of storage, and the delay between withdrawal of the blood and its examination. The in-vitro reduction of methæmoglobin in secondary methæmoglobinæmia is well recognised.[3]

1. Alexander, J. O'D. *Lancet*, 1955, i, 1201.
2. Alexander, J. O'D. *Scot. med. J.* 1958, **3**, 212.
3. Finch, C. A. *New Engl. J. Med.* 1948, **239**, 470.

In my own observations blood was taken into heparin-fluoride anticoagulant and either examined at once or stored frozen. Estimations were performed by a modification of the method of Evelyn and Malloy,[4] using a Unicam SP 600 spectrophotometer. In an earlier study[5] the method gave results in good agreement with the more rigorous techniques of gas analysis. My own experience and that of others[6] has confirmed a previously expressed opinion[5] that the Hartridge reversion spectroscope is unsuitable for observations on blood with methæmoglobin contents of less than 10% of the total hæmoglobin.

M.R.C. Group for Research on the General Effects of Radiation, Western General Hospital, Edinburgh, 4. A. G. BAIKIE.

TIGHT-COLLAR ANÆSTHESIA

SIR,—I have recently experienced an unusual symptom which I thought might interest your readers.

Several months ago I became aware of an area of anæsthesia centred over my left clavicle. It occurred from time to time during the day, and would sometimes persist for two hours, although more often it was gone in thirty minutes. There was also a vague pain and discomfort in the area.

At first I tried to ignore it, but it obtruded itself upon me so much that I had to take it seriously after a while. I thought in terms of hysteria, and, of course, multiple sclerosis, and again tried to forget it.

It was only several weeks later, when I was passing the time of day, leaning on a laboratory bench on my left elbow, that I became aware that my numbness was coming on me again, and the cause was suddenly apparent. It seemed that my shirt collar, which was a particularly stiff one, was nipping my supraclavicular nerves running over the clavicle, and causing all my troubles.

It was no doubt remiss of me not to notice that my numbness occurred only when wearing a certain shirt, but at least it was all a reminder that a very simple cause for a symptom should always be sought first.

Salisbury General Hospital, Salisbury, Wilts. RICHARD M. BEST.

FILTERED LIQUID PLASMA FOR TRANSFUSION

SIR,—The new method proposed by Dr. Ellis and Mr. Dudley[7] for use of filtered liquid plasma by ageing plus kaolin filtration is another step towards preventing homologous-serum jaundice. The first practical and safe method for achieving this result was the storage of liquid plasma at 30–32°C for six months prior to use. This discovery was made by Allen et al.,[8] whose report is cited by Ellis and Dudley. Shortly afterwards I described a simpler method.[9]

Obviously if the same procedure of ageing could be applied to dehydrated human plasma, a more stable product would be available. I believe that ageing of desiccated plasma at an elevated temperature would inactivate the virus causing hepatitis. The basis for this belief is my use of over eighty 500 ml. units of dehydrated plasma between 1949 and 1952. These units had been left in an abandoned Coast Guard hospital on Hatteras Island off the coast of North Carolina in 1946. Owing to distance and lack of communications I had to use several of these units later than the expiration date marked on the labels. These bottles of plasma had been subjected to temperatures of 37–110°F since 1946. No case of hepatitis followed. The Research Department of the National Institute of Health stated that the only objection to using this old plasma was the possible deterioration of the rubber stoppers on the bottles. These stoppers seemed in perfect condition, and I used the entire eighty units without complications. It should be noted that reconstitution of the plasma gave a clear solution.

My purpose is to arouse interest in further experimentation. Preservation of dehydrated plasma over several months will furnish a virus-free blood expander which will supersede many agents now in use.

Southport, North Carolina, U.S.A. NORMAN M. HORNSTEIN.

PHENYLBUTAZONE AND PROLAPSED INTERVERTEBRAL DISCS

SIR,—Previous letters[1 2] gave preliminary impressions of the usefulness of phenylbutazone in the treatment of disc lesions, and further controlled investigation was recommended. I can now report my subsequent findings.

The following standard procedure was adopted:

Bed rest for 10 days with 5 ml. (1000 mg.) of intramuscular phenylbutazone, and later 3 ml. (600 mg.) every other day, followed, after discharge, by twice-weekly doses of 600 mg. for six weeks from the district nurse. Thereafter a follow-up of three months to one year was arranged.

60 patients with prolapsed lumbar discs and 8 with prolapsed cervical discs were treated with intramuscular phenylbutazone and compared with a similar number of controls (treated by conventional methods and taken at random from hospital records).

All patients in both series had most of the accepted symptoms and neurological signs of disc disorder, and 25% had positive X-ray findings. If the diagnosis was still in doubt the spinal fluid was analysed, and helped on two occasions to exclude neoplasm of the vertebræ. The groups were closely matched as regards age, sex, occupation, and environment.

The results are shown in tables I and II:

TABLE I—COMPARISON OF PHENYLBUTAZONE AND CONVENTIONAL TREATMENT IN LUMBAR-DISC LESIONS

—	Without phenylbutazone	With phenylbutazone
Total no. of patients	60 (100%)	60 (100%)
First relief after:		
Two days		22 (36%) } 50 (83%)
Four days		28 (47%) }
One week	9 (15%) } 26 (44%)	
Two weeks	10 (17%) }	
Three weeks	7 (12%) }	
Relief after two weeks	19 (32%)	
Complete relief	15 (25%)	
Moderate relief	4 (7%)	
Relief lasting longer than:		
Two weeks	3 (5%)	
Four weeks	2 (3½%)	
Six weeks	12 (20%)	50 (83%)
Two months	9 (15%)	
No prolonged relief	23 (38%)	} 10 (17%)
No relief at all	11 (18%)	}
No. of relapses between six weeks and three months	3 (5%)	13 (22%)
Complete relapse		7 (12%)
Slight relapse		6 (10%)
Other treatments given:		
Lumbosacral support	10 (17%)	
Operation	7 (12%)	
Plaster	9 (15%)	

TABLE II—COMPARISON OF PHENYLBUTAZONE AND CONVENTIONAL TREATMENT IN CERVICAL DISCS

—	Without phenylbutazone	With phenylbutazone
Total no. of patients	8	8
First relief after:		
Two days		2
Four days		4
Relief after two weeks:		
Moderate relief	3	
No prolonged relief	1	
No relief at all	4	2
Other treatments given (plaster)	5	2

4. Evelyn, K. A., Malloy, H. T. *J. biol. Chem.* 1938, **126**, 655.
5. Baikie, A. G., Valtis, D. J. *Brit. med. J.* 1954, ii, 73.
6. Newcombe, C. P., Dawson, J. *ibid.* 1958, i, 1396.
7. Ellis, D., Dudley, H. A. F. *Lancet*, 1958, ii, 1355.
8. Allen, J. G., Emerson, D. M., Barron, E. S. G., Sykes, C. *J. Amer. med. Ass.* 1954, **154**, 103.
9. Hornstein, N. M. *ibid.* p. 854.

1. Steer, C. *Lancet*, 1956, i, 966.
2. Gillhespy, R. O. *ibid.* p. 1069.

It has been proved that the nucleus pulposus erupts through a tear in the annulus fibrosus under the posterior longitudinal ligament in all disc lesions. The prolapsed portion can return spontaneously, and this accounts for sudden improvements despite therapy. Herniation of the nucleus pulposus can occur only in hyperextension or overloading of the vertebral column. Quite often, however, the luxation of the protruded part persists and accounts for the protracted symptoms. When the disc becomes adherent to extradural nerve-roots, treatment with phenylbutazone or other methods is ineffective, and only an operation gives hope of cure.

I submit these results as an attempt to provide a controlled study of therapy in an admittedly complex syndrome. I have been disappointed that others have not responded to Steer's original plea for a full-scale controlled study of disc lesions treated with phenylbutazone.

Dudley Road Hospital,
Birmingham. R. O. GILLHESPY.

LUPOID HEPATITIS AND THE HEPATIC LESIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS

SIR,—The article by Dr. Mackay and his colleagues (Jan. 10) brings to light a new explanation for a puzzling syndrome. My interest in this syndrome was aroused by a fascinating case.

A 46-year-old Puerto Rican housewife in 1945 developed severe intermittent chills, weakness, and associated pain and swelling of her joints. These episodes recurred for a year and she was thereafter symptom-free until 1953 when she experienced an episode of swelling of her face, eyelids, and body which was successfully treated by her family physician. In 1957 she developed asymptomatic jaundice with associated dark urine and grey stools, which persisted intermittently until her admission to hospital. In the year before admission she lost 30 lb. in weight, and became increasingly irritable and easily fatigued; and she entered the hospital in October, 1958, on account of progressive anorexia and weakness.

There were moderately icteric scleræ; spider angiomata of trunk and forehead with scattered areas of facial hyperpigmentation; a tender, firm liver enlarged 10 cm. below the costal margin in the right midclavicular line; and a tender enlarged spleen felt 2 cm. below the left costal margin.

Laboratory examinations revealed bromsulphalein of 68% retention in 5 minutes and 33% retention in 45 minutes; icteric index 9–11; thymol turbidity 8–9; total protein 6·3 mg. per 100 ml. (albumin/globulin ratio 4·0/2·3); alkaline phosphatase ranging from 25·2 to 32·6, and total bilirubin ranging from 1·3 to 4·1 mg. per 100 ml. Hæmogram was normal, and urinanalysis was normal save for persistent bilirubin. Lupus-erythematosus-cell preparations, using the heparin method, were consistently negative. Open liver biopsy was performed, and sections revealed changes consistent with postnecrotic cirrhosis.

The patient was treated with vitamin supplements and high-calorie, high-protein diet throughout her stay in hospital, and was discharged slightly improved after a week. Since October she has done well at home without any symptoms.

This case fits into this category of lupoid hepatitis in many respects. Yet it is atypical in that no lupus-erythematosus cells could be demonstrated; that the duration of symptoms has been over fourteen years and the patient does not appear to be going downhill; and lastly that steroid therapy has not been needed. The thought has been raised by many who saw the patient that this case represents a mild form of this disease, but one which has been recognised only in recent years.

State Medical College of New York,
Kings County Hospital,
Brooklyn, New York. ARI KIEV.

CHILDREN IN HOSPITAL

SIR,—I find it difficult to understand how Sir Harry Platt (Feb. 28) has read into my letter an accusation that his committee " wished to see the . . . breaking up of children's hospitals ". If such an interpretation has been general, may I hasten to withdraw and apologise? I am very glad, however, to see his disclaimer, for Lord Cohen stated categorically in the House of Lords [1] that to break up Queen Mary's and to distribute the acute cases around adult hospitals would " conform to the desiderata of the Welfare of Children in Hospital Committee's Report".

I fully appreciate, and applaud, the *purpose* of paragraph 34, which was, I think, to make the point that even in some of the very small existing units much can and should be done to improve the welfare aspects of the care of sick children. As soon as I read this paragraph, however, I felt certain that it would be used to suggest that there was little to choose in efficiency between large and small units; and this is what happened. Lord Cohen and Lord Taylor both quoted the Platt Committee in support of the view that children's hospitals are no better than the children's wards of general hospitals for the treatment of acute cases, in flat contradiction of the Royal College of Physicians' report, and I think that this use of the report would have disturbed Sir Harry Platt had he listened to the debate.

I found the latter part of Sir Harry Platt's letter the more disturbing, because it reveals an ignorance of fact about the current work of the largest general children's hospital in the country, which is surprising in the chairman of the Platt Committee. I am glad to hear that he knew Queen Mary's in its " heyday " as a long-stay hospital under Dr. Pugh. He quite clearly does not know it now. Like many others who knew the hospital 20 or 30 years ago, he assumes that we are treating merely the disappearing rump of the very long-stay cases in the care of which the hospital became famous.

In fact Queen Mary's has moved imaginatively with the times as Lord Cohen felt that we should all do,[1] and now provides not only for the diminishing number of long-stay cases for an ever-widening area (a few come even from Wales and the North), but also a full range of acute medical and surgical services for the dense population of 1–2 million which immediately surrounds us. In 1957 80% of the cases were in for less than 2 months and 75% for less than 1 month.

If the Ministry would agree to concentrate the acute services for the area here (we already provide for at least half), the children of the area would get the best possible service, the hospital would be used to capacity, and 300 urgently needed beds, at present not much over half full, would be released for adult use in adult hospitals. In 5 years we have been unable to get this proposal seriously discussed either at board or Ministry level. In the House of Lords the only argument brought against this proposal by the Government spokesman, Lord Onslow, was that it would make parental visiting difficult. This argument was factually demolished by Lord Crook in his reply.

Sir Harry Platt may think that I advocate this course only because I am here. Actually, I am here because I advocate this course. I came here in 1953 with the advice and encouragement of the late Sir James Spence, looking into the future, not into the past, because I could see that the best way of providing for the diminishing number of sick children in very densely populated areas was to combine acute and long-stay services side by side. I was assured at the regional board that I would have their support, and, as Lord Crook showed in the House of Lords, the board did in fact do everything possible within the limits of its resources to help in this direction, in terms of establishment, maintenance, and capital expenditure between 1948 and 1958.

The Platt and Royal College of Physicians reports, dealing with welfare and organisation respectively, are complementary, and are not in real conflict at any point.

1. *Hansard*, House of Lords, Feb. 12, 1959, col. 185.

The Minister should read them side by side, not just to pick out paragraphs which suit the current trends of his administrative machine, but in order so to plan, in cooperation with the Minister of Education, that as our 80% of obsolete hospitals are rebuilt and resited over the course of the next generation, the provision for sick children comes slowly to accord, as closely as the density of population of any given area will allow, with the ideals set forth in these two reports.

No overall plan in which areas of different population density are similarly treated will do. Each area will have its own problems and its own solutions. The two reports do, however, point inevitably to the provision, in those few areas where population density is high enough, of large children's hospitals catering for acute cases from the immediately surrounding area, and for long-stay cases from further afield. It is in such hospitals that the highest standards of medical and nursing treatment, of welfare, and of education can be provided. And it is upon these few hospitals that the children's services of the country as a whole must rely for the development of ideal standards, for the further advance in knowledge of children's diseases, and for the output of those specialised children's nurses whose provision in sufficient numbers is so essential for the proper nursing of sick children whether in children's hospitals or in the children's wards of adult hospitals.

Queen Mary's is, in fact, now in a new " heyday " as a general children's hospital, and if Sir Harry Platt would pay us the honour of a visit, as I hope he will, I think he would agree that the interests of the children in this area would best be served, and his committee's recommendations most fully implemented, if the children's hospital services of this area were concentrated upon Queen Mary's.

Queen Mary's Hospital for Children, Carshalton, Surrey. DAVID LAWSON.

NEW-TYPE OXYGEN CYLINDERS: A WARNING

SIR,—I was amazed at a remark in Dr. H. M. Bird's letter of Jan. 31, 1959: " Fortunately the patient was not on controlled respiration, or he might well have died." It seems to me that every qualified physician, and particularly one who administers anæsthetics, should be able to apply effective artificial respiration to an apnœic patient without the aid of a gas machine whenever the need arises!

" For Breath Too is Nutrient " (Meneely [1]) should never be forgotten, whether the apnœic victim has been dragged from the water, struck down in the street, partially buried in a cave-in, or rendered apnœic by the administration of curare. Of all the physicians who should be able to support the life of an apnœic patient, the anæsthetist should be the last to be dependent entirely on a gas machine in order to prevent a patient from dying because controlled respiration is used and the machine suddenly becomes useless for administration of oxygen.

Blowing air intermittently through an oral airway, or directly into the mouth of the victim while pinching the nose and supporting the mandible, should always be performed promptly until efficient mechanical devices can be applied, or until the victim has restarted spontaneous adequate breathing. If mouth-to-airway or mouth-to-mouth artificial respiration is kept in mind always, no anæsthetised patient's life would ever be jeopardised just because an oxygen tank became empty and a proper replacement was not available, or did not fit the machine.

1. Meneely, G. R. *Amer. J. Med.* 1955, **19**, 323

Reticence or even repulsion from applying one's mouth to that of an apnœic, but otherwise relatively well, patient should never be a consideration when a human life is involved.

Department of Anæsthesia, University of Saskatchewan, Saskatoon, Canada. ALLEN B. DOBKIN.

THE FŒTAL ELECTROCARDIOGRAM AS A MEANS OF MINIMISING IRRIDIATION OF THE FŒTUS IN UTERO

SIR,—In view of recent appreciation of radiation hazards, the tendency is to decrease irradiation of the fœtus in utero to as little as possible. X-ray examination in suspected multiple pregnancy has been a fairly routine procedure, and a similar technique is used to gain information about the position of the fœtus in difficult cases, as well as for other reasons, including diagnosis of fœtal life. The fœtal electrocardiogram with recently improved technique may prove to be an adequate alternative method, especially for diagnosis of multiple pregnancy, and particularly because it presents no radiation hazard. Methods and instrumentation have been described.[1–3]

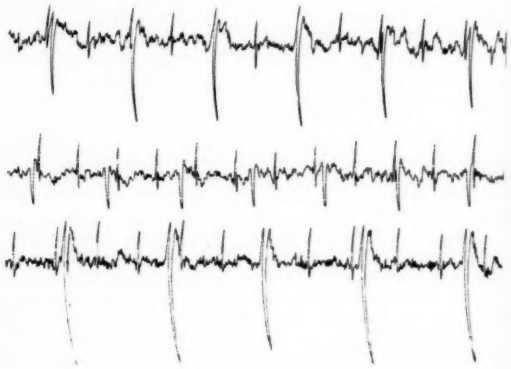


Fig. 1—Fœtal electrocardiogram in 3 normal vertex presentations. The fœtal complexes are directed up and the maternal complexes are directed down. The fœtal heart-rate is faster than the maternal.

Fig. 1 shows 3 examples of normal fœtal electrocardiograms, with the fœtus in vertex presentation. The fœtal heart-rate is seen to be faster than the maternal rate, and the fœtal QRS is oppositely directed. Fig. 2 shows the fœtal electrocardiogram in a twin pregnancy, both fœtuses presenting by the vertex. The rapid development of this technique suggests its early use for such diagnosis.

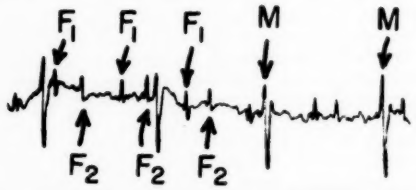


Fig. 2—Fœtal electrocardiogram in twin pregnancy. Both fœtuses are presenting by the vertex. 2 viable infants were delivered at term, both in vertex presentation.

Breech presentations give a reversed E.C.G. In a comparable

1. Larks, S. D., Dasgupta, K. *Amer. Heart J.* 1958, **56**, 701.
2. Larks, S. D. *Amer. J. Obstet. Gynec.* (in the press).
3. Larks, S. D. *in* Medical Physics; vol. 3 (edited by O. Glasser). Chicago, Ill., 1959

case of twins, both breech, the fœtal complexes would be directed downward—i.e., the maternal and fœtal complexes would be in phase.

This research was supported by a grant-in-aid from the United States Public Health Service.

Departments of Biophysics and Obstetrics and Gynecology, Medical Center, University of California, Los Angeles. SAUL DAVID LARKS.

MALARIA IN NORTH BORNEO

SIR,—I was glad to read a letter from Dr. Copeland (Dec. 6), a pioneer in bringing medical treatment to the Muruts of North Borneo.[1] I feel that something should be said about the present malaria situation there.

McArthur's control measures for the vector "*Anopheles leucosphyrus*" (now *A. balabacensis*), were in fact resumed by him under the new post-war Government. Clearing the undergrowth around seepages was tried during 1949–52, and showed some reduction in vector breeding and spleen-rates.[2] However, more recent surveys have shown that McArthur's experimental villages no longer show any malariometric advantage over comparison villages, despite his hopes for the relative permanence of his methods.

It was decided by the Government/W.H.O./UNICEF Malaria Project to use house spraying with residual insecticide, which had proved highly effective in Sarawak against the virtually identical *A. leucosphyrus*. For Dr. Copeland's information, these mosquitoes do rest on walls during the night for periods sufficiently long to make them susceptible to effective attack by residual insecticides.

It has been shown during the past three years that residual insecticides produce a very great decrease in the density of the vector. On Labuan Island house-spraying alone has been successful in interrupting transmission, and when combined with antimalarial drugs it has been shown capable of controlling transmission even in the most difficult parts of the interior. The complete eradication of malaria from British North Borneo now appears to be an attainable goal.

University of Malaya in Singapore. IVAN POLUNIN.

REINFUSION OF ASCITIC FLUID

SIR,—Greene[3] and later Girard et al.[4] reported the therapeutic use of reinfusion of ascitic fluid in patients with hepatic cirrhosis. They withdrew the fluid and reinfused 300–1000 ml. intravenously into the same patient. In some cases diuresis ensued and the ascites decreased, but there were often febrile reactions and sometimes even a shock-like state.

A significant factor in the formation of ascitic fluid, besides portal congestion, is the decreased colloid-osmotic pressure due to decrease of the plasma-protein content. The protein content of the ascitic fluid is 1–3 g. per 100 ml. It seemed logical therefore to reinfuse greater amounts of the fluid. It is also advantageous to the patient to get his own proteins back.

In 1951 one of our patients with hepatic cirrhosis, a 38-year-old man, did not improve despite the usual treatment, and we were compelled to withdraw every three weeks 8–10 litres of ascitic fluid. The continued withdrawals enhance the patient's cachexia. Accordingly we tried the intravenous reinfusion of his ascitic fluid. The first infusion (800 ml.) provoked fever and indisposition; therefore we reduced the amount to 150–300 ml., and this gave rise to no reaction. The patient received in six and a half months 36 reinfusions, which in the beginning were given every second to third day, finally once a week. After six to ten reinfusions diuresis increased, the general condition improved, and the ascites began to diminish; it disappeared finally. The size of the liver and spleen decreased. The patient has since been in a good condition without ascites. His serum-proteins increased from 5·2 (albumin 2·8, globulin 2·4) to 6·8 (albumin 4·3, globulin 2·5) g. per 100 ml., and the albumin/globulin ratio from 1·16 to 1·7.

We have since applied this treatment in 9 cases. In 1 case there was an excellent result, in 4 cases some improvement, and in 4 no improvement.

We want to stress the following observations:

1. It is advisable to use fresh ascitic fluid. In old ascitic fluid the proteins and other organic compounds become denatured in the abdominal cavity to some extent and may cause fever and other reactions.

2. The intravenous reinfusion of small amounts of ascitic fluid is not substitutional therapy, but constitutes a stimulus for the formation of new blood-proteins. In cases which respond, the hypoalbuminæmia disappears and the albumin/globulin ratio is restored to normal.

3. The prognosis in cases which do not react with an increase of the blood-proteins seems to be unfavourable.

II Medical Clinic of the University of Budapest, Hungary. L. A. PÁLOS, Z. ANTALÓCZY.

BRACHYMETACARPAL DWARFISM

SIR,—Dr. van der Werff ten Bosch is to be congratulated on the clear-thinking article (Jan. 10) in which he discusses several obscure developmental defects, and groups together eight cases in which there are dwarfism and disturbance of metacarpal growth. The factor common to all these cases is that they show abnormal growth of *some* bones—or, to put it another way, they show *normal* growth in some bones. Thus, as far as the skeleton is concerned, the condition presumably cannot be caused by a central disturbance, whether endocrine or metabolic; it seems much more likely that it is due to a fault in the development of the stunted bones themselves. The stunting could well be the result of premature cessation of growth in the affected growth cartilage plates, an event which would be followed by their vascularisation and ossification. If this suggestion is borne out by further investigation, the condition might better be grouped among the dyschondroplasias; furthermore, one might hazard a guess that human growth hormone will not induce normal growth in these patients.

Trinity College, Dublin. ROY M. ACHESON.

CORTICOTROPHIN IN HÆMOLYTIC ANÆMIA

SIR,—In 1952 my article entitled A.C.T.H. in Clinical and Experimental Hæmolytic Anæmia appeared in *The Lancet*.[1] There were, however, some serious faults in the animal experiments—e.g., the hæmolytic antisera injected into the guineapigs were not the same serum but different sera though of similar titres (this was not stated in the paper). Also the results on the second of 2 corticotrophin-treated rabbits and the second of 2 corticotrophin-treated guineapig should be disregarded. 2 of the control guineapigs were overweight also. Further details on less severe inaccuracies can be supplied if necessary.

I have repeated this work with unsatisfactory results. I was wondering if it would be possible to issue a correction with regard to two of the conclusions—i.e., changing the claim that corticotrophin has no effect on developing hæmolytic antibodies in rabbits and also does not affect the hæmolytic anæmia in guineapigs caused by hæmolytic antisera to a statement saying that the results were inconclusive. The corticotrophin appeared to be potent.

97 General Hospital, APO 757, Frankfurt, Germany. K. P. CLEARKIN.

1. Copeland, A. J. *Lancet*, 1935, i, 1233.
2. McArthur, J. *Trans. R. Soc. trop. Med. Hyg.*, 1954, **48**, 234.
3. Greene, C. H. *J. Amer. med. Ass.* 1943, **121**, 715.
4. Girard, M., Fraisse, H., Chabanon, R. *Arch. Nat. Appar. Dig.* 1949, **38**, 910.

1. *Lancet*, 1952, i, 183.

NEUROTIC DISTORTION OF THE CREATIVE PROCESS

SIR,—Your review [1] of this book by me contains two flagrant distortions.

In the book I state repeatedly that it is not my intention to present evidence, but merely to make a complex hypothesis clear and understandable, and to illustrate it with examples. In spite of this you say that the book " will certainly convince the converted ". This bit of sarcasm is both snide and misleading. You need not have read beyond p. 4 to find the following sentence: " If I can succeed in presenting an hypothesis which will clarify even a small part of this, and which can ultimately be subjected to clinical and experimental validation, my major purpose will be achieved."

Similarly, you would not have had to read beyond p. 5 to find my unequivocal statement that in the problems of creativity *as in all other* problems, psychoanalytic therapy " succeeds only under certain . . . circumstances and fails under others "—a statement which I amplify further in the same paragraph, and in others. In spite of such unequivocal disclaimers on my part, you ascribe to me assumptions about therapy which are alien to a point of view which I have expressed repeatedly both in this and in other publications.[2 3]

New York, N.Y. LAWRENCE S. KUBIE.

Parliament

Local-authority Domicile

THE National Assistance Act 1948, as at present worded, may put an unfair burden on a local authority which has in its area hospitals which receive patients from outside its boundaries. During a stay in hospital, especially if it happens to be a long stay, a patient may give up his former home. If this happens, the responsibility for providing him with residential accommodation on discharge falls on the authority of the area in which the hospital is situated. The National Assistance (Amendment) Bill, a private member's measure, which was read a second time on Feb. 27, seeks to apportion this responsibility more fairly. It provides that patients who need local-authority accommodation on leaving hospital will be regarded as living in the area from which they entered the hospital and will remain the responsibility of that authority. The Bill also provides that a local authority should not be responsible for providing welfare services for disabled people who have moved into the area because there is a sheltered workshop in it.

QUESTION TIME

Chiropody in the N.H.S.

IN answer to a question Mr. DEREK WALKER-SMITH announced that he was now ready to approve proposals by local health authorities who wish to provide a chiropody service as part of their arrangements for the prevention of illness under section 28 of the National Health Service Act. He proposed to consult the local authority associations immediately on the terms of a circular to be sent to the authorities.

Mr. J. A. KERSHAW: Can the Minister indicate what categories of people will be able to benefit by this; and will he give an assurance that the very considerable labours of voluntary organisations will not be lost as a consequence of this new step?—Mr. WALKER-SMITH: The first part of the supplementary question is a matter for the individual local health authorities, but I intend to ask them to give priority in the early years of the new service to the elderly, physically handicapped, and expectant mothers. As to the second part concerning voluntary bodies, from April 1 local health authorities wishing to contribute to the funds of voluntary organisations under section 28 (3) for the purposes of providing chiropody will not need to seek my approval to do so.

1. *Lancet*, 1958, ii, 1103.
2. Kubie, L. S. *in* Progress in Psychotherapy; p. 87. New York, 1956.
3. Kubie, L. S. *J. ment. Sci.* 1958, **104**, 518.

Registration of Chiropodists

Mr. ARTHUR BLENKINSOP asked the Minister whether he would make a further statement regarding the registration of chiropodists and the use of fully qualified chiropodists in a national chiropody service for old people.—Mr. WALKER-SMITH: I have in draft a scheme for the registration of medical auxiliaries (which includes the registration of chiropodists) on which I am further consulting the medical profession. Meanwhile the qualifications of chiropodists employed in the National Health Service are governed by statutory Regulations. Mr. BLENKINSOP: In view of the announcement that the Minister has made about the development of the chiropody service, is it not desirable to press on more rapidly with the registration of chiropodists?—Mr. WALKER-SMITH: I should be very reluctant to abandon the attempt to have a general registration scheme in respect of medical auxiliaries and have to embark upon piecemeal legislation for the various classes of auxiliary.

Smoking and Lung Cancer

Mr. SOMERVILLE HASTINGS asked the Minister whether, in view of the steadily increasing death-rate from cancer of the lung, and the need for direct evidence and an authoritative statement as to the relationship between smoking and this disease, he would recommend the appointment of a Royal Commission to inquire into the matter.—Mr. WALKER-SMITH: This is a matter for scientific research and assessment, rather than for a Royal Commission. In 1957 the Medical Research Council made an authoritative assessment of the evidence then available, and research is continuing. Mr. HASTINGS: Does not the Minister realise that the public is waiting for an authoritative statement by an independent body and perhaps rather suspects doctors and the other members of the Medical Research Council? The public is being told one thing by the Medical Research Council and something quite different by the tobacco manufacturers, and it wants to know what is true. Would it not be useful to set up a Royal Commission of responsible men and women to come to some conclusion and let the public know the truth?—Mr. WALKER-SMITH: I would be sorry to think that the public was suspicious of doctors in this or, indeed, in any other context. On medical and scientific questions, it is advisable to have regard to the careful assessments made by doctors and scientists. The Medical Research Council, in a statement in 1957, concluded that it was reasonable to associate a major part of the great increase in lung cancer with tobacco smoking. No new information of major significance has come to hand since then, but there have been follow-up reports from various countries that have tended to confirm that assessment.

Attempted Suicide

Mr. KENNETH ROBINSON asked the Home Secretary what further progress he had made in his discussions with regard to the law relating to suicide. Mr. R. A. BUTLER replied: I am pursuing, in consultation with the Minister of Health, my study of the question how, if attempted suicide ceased to be a criminal offence, we could ensure that people who attempted to kill themselves and were in need of mental treatment would in fact receive it. We have obtained information about the way in which this problem is dealt with in other countries, and a meeting will shortly take place between officers of my Department and representatives of the joint committee of the British Medical Association and the Magistrates' Association which has considered this subject.

Cost of Analysis not Deductible Expense

Mr. KENNETH ROBINSON asked the Chancellor of the Exchequer why, when a psychiatrist underwent a training analysis to increase his therapeutic skill, no part of the cost of such an analysis was allowed as a deduction from income for income-tax purposes.—Mr. D. H. AMORY replied: If the question relates to psychiatrists in salaried employment assessed under schedule E, the cost of personal analysis is not regarded as satisfying the test laid down by law, which is that expenses are

deductible only if incurred wholly, exclusively, and necessarily in the performance of the duties of the employment.—Mr. ROBINSON: Is the Chancellor aware that the purpose of this analysis is solely to make a man a better doctor? Is he aware that many younger psychiatrists are spending as much as £500 a year—perhaps a third of their gross salary—on these courses in the interests of their patients?—Mr. AMORY: I do not disagree with what the hon. Member has said about the importance of this training, but, as he knows, the test in the case of employed persons under schedule E is very strict, and these courses, deserving as they are, do not seem to amount to an essential qualification for employment.

Radiation Hazards

The Health Ministers have received an interim report from Lord Adrian's committee on this subject. It deals mainly with mass miniature radiography, the value of which the committee consider far outweighs any effects of the very small amount of radiation involved. It also includes some preliminary observations on radiological procedure generally.

Obituary

WILLIAM JAMES STUART

C.B.E., M.A., M.B. Edin., F.R.C.S.E.

Mr. W. J. Stuart, senior consulting surgeon to the Royal Infirmary, Edinburgh, died on Feb. 22 at the age of 85.

His father, the Rev. John Stuart, was the minister of St. Andrew's Parish Church, Edinburgh, and his mother was the daughter of James Duncan, M.D.

His education started at Edinburgh Academy, where he finished as gold medallist and dux of the school. At the University of Edinburgh he continued to collect distinctions, and he graduated M.A. in 1894 and M.B. with honours in 1899. He held several resident appointments in the Royal Infirmary, and became F.R.C.S.E. in 1903. After a period as private assistant to Prof. John Chiene, he studied at surgical clinics abroad, spending several months with Professor Kocher.

In 1906 he was appointed assistant surgeon to the Deaconess Hospital, and two years later assistant surgeon to the Royal Infirmary. During the 1914–18 war he served as a Territorial officer in the R.A.M.C. at home and in Salonika until 1918. He retired from the staff of the Royal Infirmary in 1938, but the late war brought him back to take charge of surgical wards for a further three years.

In 1937 he was elected president of the Royal College of Surgeons of Edinburgh, and in 1944 he became president of the Medico-Chirurgical Society of Edinburgh. For some years he was chairman of the executive committee of the Scottish National Blood Transfusion Association and of the Edinburgh Cripple and Invalid Children's Aid Society. He was a senior member of the kirk session of St. Andrew's Parish Church, and took a notable part in social work, including the Edinburgh Medical Missionary Society and the Y.M.C.A. He was appointed C.B.E. in 1952.

As a young man he had a distinguished athletic record in rugby, cricket, and hockey, and when he was well up in his fifties he continued to open the batting for the Royal Infirmary staff in the annual cricket match against the residents. He was a lifelong devotee of the gun and rod, but admitted somewhat reluctantly that in his eighties he found the high moors and mountain lochs " rather tiring ".

R. I. S. writes:

" Pussy was the name by which Stuart was universally known. Given in his youth to denote his gentleness, the passing years emphasised its appropriateness; he was above all a gentle man. He never owned a motor-car, but during the whole of his professional life rode a bicycle. The tall, erect figure pedalling with great dignity was a familiar and cherished sight in the streets of Edinburgh.

" As an orator, he had few equals. No-one who heard it can ever forget his presidential oration and toast to the Immortal Memory of Harvey, nor the ovation which it evoked. He maintained his interest in the classics throughout life, and, as a close friend remarked at the time of the oration, Pussy could have delivered it with equal facility in Latin or in Greek. Spartan in the conduct of his own life, he was indulgent to the foibles of others. His unswerving rectitude made him stand firm on any moral issue, but his judgments were never harsh. He could find something good to say of everyone, and the very fact seemed to bring out the best in them.

" His patients regarded him with confidence and devotion. To him their general welfare was of as much interest as their surgical condition. As a teacher he was brilliant, as a surgeon very sound, but both attributes were subordinate to his impact as a man. His extraordinary untiring devotion to duty whatever the cost, his modesty, kindliness, tolerance, and unfailing courtesy to the highest and lowliest made a lasting impression on all with whom he came in contact. His students and residents acknowledged him as one of the great formative forces in their lives, and his correspondence with them years later was voluminous. Two months before his death his former residents and associates gave a dinner in honour of his 85th birthday. He delighted all with a witty speech, full of reminiscences and subtle leg-pulling, delivered with much of his pristine vigour. In the course of it he remarked that he had had a full life and did not object to growing old—then he paused and gazed ahead as one who made a landfall. Can we doubt that for this ' gentleman unafraid ' it was a good one? "

THOMAS PEARSE WILLIAMS

M.D. Lond., F.R.C.P.

Dr. Pearse Williams, who was appointed honorary consulting physician to Paddington Green Children's Hospital and to Willesden General Hospital on his retirement from their staffs last year, died on Feb. 22 at the age of 65.

He was born in Plymouth, where his father was a general practitioner. He was educated at Plymouth College and the Middlesex Hospital Medical School, where, like his father, he held a Broderip scholarship. After qualifying in 1916 he joined the R.A.M.C., and served in India. On his return he held medical registrarships at St. Mary's Hospital and at the Middlesex Hospital. In 1921 he was appointed physician to outpatients at Paddington Green Children's Hospital, and he was made a full staff member in 1927. He was appointed consultant physician to Willesden General Hospital in 1926.

For 18 years he was a member of the executive committee of Willesden General Hospital, and he had the rare distinction of being chairman from 1941 to 1948—an unusual office for a doctor to hold. After the introduction of the National Health Service he served on the Central Middlesex Group hospital management committee until 1954. He was the first president of the Willesden General Hospital Medical Society, founded in1954, and on his retirement in 1958 the society presented him with his portrait by David Craig. From 1924 to 1951 he was medical officer to the Polytechnic, and he was for many years visitor for the Middlesex County Council under the Mental Deficiency Acts.

A colleague writes:

P. W. will be remembered by many younger physicians for all he taught them of courtesy and kindness. The care of his hospital patients was his prime concern, and he was more interested in good common sense and clinical observation

than in rare laboratory tests. Yet he was never scornful and always glad for a new investigation to be carried out, so long as there was a good reason and the possible advantage would clearly outweigh the discomfort to the child. He must have been one of the best of the old and, unfortunately, disappearing true clinicians; he was as good (and this means excellent) at adult medicine as at pædiatrics. He was not a prolific writer and used to say with his gentle smile how he had noticed some readers of the journals first looking to see whether their names were mentioned in the list of references before they read the article. He abhorred verbosity and considered that the multiplication of paper work was a great ill. In committee during his last few years of active professional life he was reluctant to express his own ideas about the future since his retirement was near, but his colleagues, both young and old, came to value and seek his advice more and more. He certainly was at his best in the small hospital where personal relations are so important and where he contributed so much to ensure that all felt happy and useful and hence were doing their finest work. He neither liked, nor entirely approved of, big departments where there is less of the intimate give-and-take between house-physician and consultant—and he would have put them in this order."

Dr. Pearse Williams was twice married, and his second wife survives him.

ARTHUR GEORGE PHEAR

C.B., B.A., M.D. Cantab., F.R.C.P.

Dr. A. G. Phear, consulting physician to the Royal Free Hospital, died on Feb. 26 at the age of 91.

He was born at Croydon, the son of Henry Carlyon Phear, and educated at Charterhouse, Trinity College, Cambridge, and University College, London. After taking a first class in the natural sciences tripos in 1888 he graduated in medicine in 1891. Having held house-appointments at U.C.H. he became assistant to the Holme professor of clinical medicine in the medical school, and one of his earliest publications was a joint paper with Sydney Ringer on the influence of saline media on the tadpole. He held a clinical assistantship at The Hospital for Sick Children, Great Ormond Street, and then joined for a time the staff of the Metropolitan Hospital. Later he was associated with the Royal Chest Hospital in London and the Royal National Hospital for Consumption at Ventnor. But the Royal Free Hospital, to which he was appointed in the early years of this century, and the London School of Medicine for Women, where he held a lectureship, remained the centre of his practice and his interest.

In 1902 he was elected F.R.C.P., and he acted as examiner for the college, as well as for the Universities of Cambridge and London. During the 1914-18 war, though already in his fifties, he saw much service abroad as consulting physician to the British Forces in Salonika and Army of the Black Sea. For this work he was twice mentioned in despatches and appointed C.B. in 1919.

Dr. Katharine Lloyd-Williams, dean of the Royal Free School of Medicine, writes:

"By the death of Dr. Phear the Royal Free Hospital has lost one of its oldest and greatest friends. He died in the hospital after many months of illness during which he endeared himself to yet another generation of nurses and house-officers. When my own generation of students were at the Royal Free soon after the 1914-18 war, Dr. Phear still had for us the romantic aura associated with those who had taken part in that epic struggle, more especially with those whose work had been part of the often tragic events in Salonika and Greece. He was even then of an age when many doctors might think that service at home was all that should be asked of them. But his activities were not restricted by age. Where service was needed there he would be.

"He held the post of senior physician at the Royal Free Hospital from 1922, and the appointment as house-physician to his firm was one of the most eagerly sought in the hospital. This was not only because of his eminence as a teacher, which was unrivalled, but also because of the opportunity it gave to be in close association with a physician of the highest professional integrity. As students his quizzical kindliness and tolerance of our faltering inadequacy did not disguise from us the knowledge that he expected in return the best we were capable of producing. His own standard of service was an ideal for which we were bound to strive. His influence on students in a quiet way was immense, and his interest in them, and their careers and lives, unfailing.

"He and his wife were endlessly hospitable and a party at his house delighted students for the opportunity it gave them of hearing his almost professional playing of classical music. This interest remained to the end, and he entertained some of us on his 85th birthday by playing on the harpsichord. In 1958 he gave an organ to the chapel at the Royal Free and in 1959 his own piano to the nurses' home—generous gifts which are a lasting memorial to him.

"He was an erudite man with wide interests and his mental capacity seemed really untouched by his years. A visit to him in hospital and the chance of a conversation with him remained to the end a real mental stimulus. He loved the Royal Free Hospital, and those of us who had the good fortune to know him well had the greatest admiration and affection for him. He was essentially modest, and perhaps never realised how much we knew we owed to him."

Dr. Phear married in 1897 Ellen Frances, daughter of the late Arthur Lister, F.R.S.

Our photograph is taken from Muriel Jackson's study of *Dr. Phear at the Clavichord*.

WILLIAM WASHBOURN

C.B.E., M.R.C.S.

Mr. William Washbourn, consulting surgeon to the Gloucestershire Royal Infirmary, died at Blackfriars, Gloucester, on Feb. 4 at the age of 96.

Born in Gloucester, he came from a family that could trace its origin back to the Conquest and took their name from the villages of Great and Little Washbourn, near Broadway, Worcestershire. They went to Gloucester when they were dispossessed of their lands in Cromwell's day and became clockmakers, and perhaps it was from them he inherited his manual dexterity. He was educated at the King's School, Gloucester, and became a "pupil" at the General Infirmary at Gloucester in 1880. Later he went to University College London, and qualified in 1885. He held a house-appointment at University College Hospital and spent a short time in Germany before he returned to Gloucester to become house-surgeon at the Infirmary. He was appointed assistant surgeon in 1894 and full surgeon in 1898. As was customary in those days he also did general practice, and he was a master of the art of prescription. For many years he was deputy coroner for the city and medical assessor to the county court. In the 1914-18 war he took charge of the Red Cross hospital in Gloucester, and also sat on medical boards. For these services he was appointed C.B.E. On his retirement from the staff in 1924 he was made vice-chairman of the Gloucestershire Royal Infirmary, as it had then become, and during the late war was its acting chairman. He retired when the National Health Service was introduced, after an association with the Infirmary of 67 years, ranging from "pupil" to chairman.

E. N. D. writes:

"Washbourn was a brilliant surgeon. Though brought up in the Listerian tradition of antiseptic technique, he soon adapted himself to the new aseptic methods. He worked in the days when operations were performed in the patient's home with the aid of oil-lamps and kitchen tables, and stories of his prowess and powers of improvisation under these conditions are still told. From his brother, Dr. J. W. Washbourn, he acquired an interest in pathology and bacteriology, and he cut all his own sections from his operation specimens, and did his own bacteriology and also that of the city of Gloucester. He remained to the end a good opinion on a histological slide.

"Despite all his medical activities he was an open-air man. He never wore an overcoat—it is doubtful if he possessed one—and he could be seen on the coldest day taking his regular walk beside the river Severn. He was the oldest surviving playing member of the famous Gloucester Rugby Club. A fine shot, he won many prizes at Bisley. But it was as a dry-fly fisherman that he was most renowned, tying all his own fly and making them with feathers he had dyed himself. He was an early motorist and the first motor-car licence-holder in Gloucester. He always did his own car repairs and once, during the late war, when approaching 80 years of age, fitted a new big-end to his car. His long life spanned a complete revolution in the ways of conventional living, and in the practice of medicine and surgery, and he was great enough to take it all in his stride."

He married Mabel Wood Collins in 1910, and she survives him with their only son.

IVOR ELWYN JOSEPH THOMAS

M.D. Lond., M.R.C.O.G.

Mr. Ivor Thomas, consultant obstetrician and gynæcologist to Pembury Hospital, died on Feb. 23 at the age of 45.

After qualifying from Guy's Hospital in 1937, he held junior appointments there, including those of resident obstetrician and obstetric tutor to the medical school. In 1939 he went to Pembury Hospital with the E.M.S. team from Guy's. Apart from his service with the R.A.F., he remained there for the rest of his life, becoming a consultant gynæcologist and obstetrician when the health service was started.

E. D. Y. writes:

"I knew Ivor Thomas from his early days at Guy's and was delighted to count him as a friend and to welcome him as a colleague. He was modest and kind, always courteous to his patients, and a well-loved colleague. As a surgeon he was skilful, sure, and meticulously careful, and his ability was matched by wide knowledge of his subject. After he fell ill in 1957, he continued, despite considerable pain and discomfort, to carry out his hospital work with selfless courage."

Mr. Thomas leaves a widow.

Appointments

BRODBIN, Patrick, L.R.C.P.I., D.P.H.: M.O.H., Hucknall.
COUCH, R. S. C., M.D. Lond., M.R.C.P., F.F.R., D.M.R.D.: assistant radiologist (consultant), Royal National Throat, Nose and Ear Hospital, London.
FLEETWOOD, H. G., M.B. Manc.: senior school M.O., Stoke-on-Trent.
GREEN, R. I., M.D. Lpool, D.M.R.D.: consultant radiologist, Clwyd and Deeside H.M.C. area.
SCOTT, JEAN M., M.D. Glasg.: assistant pathologist, Glasgow Royal Maternity and Women's Hospital.
THOMPSON, BEATRICE M., M.D. Lond., D.P.H.: senior M.O., maternal and child health services, Somerset.

Birmingham Regional Hospital Board:

BOURNE, W. I. H., M.B. Birm., D.M.R.D.: part-time consultant radiologist, West Bromwich group of hospitals.
CASON, J. S., M.B. Leeds, F.R.C.S.: consultant surgeon, burns unit, Birmingham Accident Hospital.
MATTHEWS, R. P., M.B. Madras: senior casualty officer, South Worcestershire group of hospitals.
THOMSON, H. R., M.D. Lond., M.R.C.P.: consultant physician (geriatrics), Coventry group of hospitals.

Diary of the Week

MARCH 8 TO 14

Monday, 9th

UNIVERSITY OF LONDON
5.15 P.M. (University College, Gower Street, W.C.1.) Prof. J. Folch-Pi (Harvard Medical School): Brain Lipoproteins and Proteolipids. (First of two lectures.)
POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
4 P.M. Dr. Brian Ackner: Psychopathic Personality.
INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Prof. W. B. Shelley: Studies in the Nature of Itching.
UNIVERSITY OF ST. ANDREWS
4 P.M. (Department of Medicine, Dundee.) Dr. William Walker, Dr. H. B. Goodall: Hypersplenism.

Tuesday, 10th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. P. L. Mollison: Blood Group Antibodies and Red Cell Destruction. (First of two Oliver-Sharpey lectures.)
ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
3.45 P.M. Mr. P. C. Williams: Hormones and Cancer (Imperial Cancer Research Fund lecture).
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Prof. G. H. Lathe: Metabolism of Bilirubin.
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. *Experimental Medicine and Therapeutics.* Prof. M. L. Rosenheim: The Professorial Medical Unit. (Presidential address.)
8 P.M. *Psychiatry.* Dr. Joshua Bierer, Dr. Arthur Pool (for); Dr. A. A. Baker, Mr. Kenneth Robinson, M.P. (against): That Most Mental Hospitals Meet the Needs Neither of Their Patients Nor of the Communities Which They Serve.
ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Dr. P. E. Hughesdon: Pathogenesis of Endometriosis.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Michael Feiwel: Skin Manifestations of Some Metabolic Diseases.
BIRMINGHAM MEDICAL INSTITUTE
8 P.M. (36, Harborne Road, Edgbaston.) *Psychiatry.* Dr. Myre Sim: Aspects of American Psychiatry.
MANCHESTER MEDICAL SOCIETY
8 P.M. (Clinical Sciences Building, York Place.) *Surgery.* Mr. W. J. Metcalfe, Mr. F. S. Mitchell-Heggs, Mr. J. P. Lythgoe, Mr. H. A. Haxton: Suturing of the Abdominal Wall.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Dundee.) Prof. Adam Patrick: Disseminated Sclerosis. (Second of two lectures.)

Wednesday, 11th

UNIVERSITY OF LONDON
5.15 P.M. (University College.) Professor Folch-Pi: Brain Lipoproteins and Proteolipids. (Second of two lectures.)
POSTGRADUATE MEDICAL SCHOOL
2 P.M. Dr. Betty Hobbs: Current Problems in the Control of Food Poisoning.
ROYAL SOCIETY OF MEDICINE
4.30 P.M. *Physical Medicine.* Dr. G. O. Storey, Dr. P. Hume Kendall, Dr. D. R. L. Newton: The Painful Shoulder.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Henry Haber: Specific and Foreign Body Granulomata.
INSTITUTE OF NEUROLOGY, Queen Square, W.C.1
5.30 P.M. Prof. Eric Kugelberg (Stockholm): Nociceptive Reflexes in Man.
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Prof. D. W. Smithers: Œsophageal Cancer.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3.30 P.M. Dr. Philip Ellman: Social Implications of Chronic Bronchitis.
MANCHESTER MEDICAL SOCIETY
5 P.M. (Medical School, University of Manchester.) *Pathology.* Dr. Simon Sevitt: Renal Failure and Tubular Necrosis in Burned and Other Patients.
UNIVERSITY OF ST. ANDREWS
4 P.M. (Department of Medicine, Dundee.) Dr. Walker: Current Studies in Blood Coagulation.

Thursday, 12th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. Mollison: Blood Group Antibodies and Red Cell Destruction. (Second of two Oliver-Sharpey lectures.)
ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P.M. Mr. Alan Parks: Micro-anatomy of the Breast. (Hunterian lecture.)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. C. L. Cope: Measurement of Adrenal Activity in Man.
ROYAL SOCIETY OF MEDICINE
5 P.M. *Ophthalmology.* Mr. E. S. Perkins, Mr. John Winstanley: Low Tension Glaucoma.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. R. W. Riddell: Control of Fungous Infections.
MIDLAND THORACIC SOCIETY
5.30 P.M. (36, Harborne Road, Edgbaston.) Dr. J. F. Bromley: Non-surgical Treatment of Intra-thoracic Malignant Disease.
WEST OF ENGLAND CHILD HEALTH GROUP
8.30 P.M. (Children's Hospital, Bristol.) Dr. Philip Evans: Baby Farming.
LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool, 3
8 P.M. Dr. R. M. Davies: Recovery Wards.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Dundee.) Prof. A. Bradford Hill: Observation and Experiment in Medicine.

Friday, 13th

POSTGRADUATE MEDICAL SCHOOL
10 A.M. Mr. W. R. Henderson: Spinal Tumours.
4 P.M. Prof. J. D. Hay: Pulmonary Stenosis in Childhood.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
5.30 P.M. Mr. Charles Heanley: Plastic Surgery of the Nose.

Notes and News

STUDENT EXPEDITION TO BELGIAN CONGO

THE prospectuses of the tourist agencies offer an embarrassment of even remoter choices every year; but, given a purpose and generous sponsors, it is still possible to travel even further. Six senior Westminster Hospital students have lately returned from an expedition to the Belgian Congo. This lasted four months, from last September to January, and about nineteen thousand miles of rough travelling were covered in a route which led through Spain, Algeria, the Sahara, and Nigeria. However, mechanical incidents were confined to three broken springs and a fractured back-axle. The expedition cost about £2000, and over 140 firms and private individuals, besides various bodies in Westminster Hospital itself, contributed financial help or gifts in kind.

One of the main objects was to study the physiology of acclimatisation. Not very surprisingly, the more elaborate investigation of fluid and electrolyte balance had to be abandoned in the conditions of the Sahara; but many recordings of less complex data, such as blood-counts and urine analysis, were obtained, and these are to be reported in detail. In the Congo itself plants were collected for an inquiry into radioactivity content, and specimens of soil were taken for assessment of their antibiotic potentialities. In a medical survey of a native village routine clinical and pathological examinations of a sample of the population disclosed much endemic disease and infestation. Fortunately, despite arduous travel through countries with various hazards, the members of the expedition remained healthy, their illnesses being limited to gastroenteritis and a single instance of " Red Congo Fever ".

In an age when students are continually accused of lacking joie-de-vivre and of conforming to a rigid pattern, it is refreshing to hear of such enterprise. Crossing the Sahara is still a formidable undertaking for the tiro, and Algeria is not without its dangers. It was not to be expected that such an expedition would make discoveries that had escaped previous, more expert, teams; but the Westminster group must have learnt much about the difficulties of scientific observation in the field, and also much about the world outside England and the particular needs of Africa.

ADDICTION AND RESPONSIBILITY

THE North-East Metropolitan Regional Hospital Board have announced that they are consulting their own medical advisory committee and the Ministry of Health about the following implications arising from the recent case when an anæsthetist was convicted of manslaughter [1]:

The alleged practice of some anæsthetists of testing anæsthetic gases by inhalation, with the possibility of adverse effect upon their capacity to undertake their professional duties.

The responsibility, if any, of hospital medical staff in relation to alleged shortcomings of their medical colleagues.

HOSPITAL BOARD CHAIRMEN

THE Minister of Health has made the following appointments and reappointments of chairmen of regional hospital boards and boards of governors of teaching hospitals:

New appointments.—East Anglian, Sir Stephen Green; Liverpool, Mr. T. W. Harley; South Western, Colonel H. A. Guy; United Liverpool Hospitals, Mr. H. S. Dickson; Welsh, Sir Godfrey Llewellyn; Wessex, Mr. P. G. Templeman.

Reappointments.—Manchester, Mr. N. M. Agnew; Moorfields, Westminster and Central Eye Hospital, Mr. C. J. Malim; National Hospitals for Nervous Diseases, Sir John Woods; North West Metropolitan, Lord Cottesloe; Sheffield, Mr. A. V. Martin; South East Metropolitan, Sir Ivor Julian; United Bristol Hospitals, Colonel H. Bland Stokes.

Sickness Absence and Its Control

The Industrial Welfare Society will hold a conference on this subject at the St. Enoch Hotel, Glasgow, on Tuesday, April 14. Further particulars may be had from the society, 48, Bryanston Square, London, W.1.

1. See *Lancet*, Feb. 28, 1959, p. 464.

University of Oxford

Dr. W. D. M. Paton, professor of pharmacology at the Royal College of Surgeons of England, has been appointed to the chair of pharmacology in succession to Prof. J. H. Burn. He takes up his appointment in October.

Dr. Paton, who is 41, graduated B.A. Oxon. with first-class honours in animal physiology in 1938. He continued his medical studies at University College Hospital Medical School, London, and after qualifying in 1942 he was house-physician to the medical unit there before he became resident pathologist at King Edward VII Sanatorium, Midhurst. From 1944 to 1952 he was a member of the Medical Research Council's scientific staff at the National Institute for Medical Research. During this period was done the work on the methonium compounds for which, with Prof. Eleanor Zaimis, he was later awarded the Cameron prize of the University of Edinburgh, and one of the first awards of the Gairdner Foundation of Toronto. In 1952 he was appointed reader in applied pharmacology at University College and U.C.H. Medical School, and the following year he took the D.M. He was appointed to his present chair, its first holder, in 1954. In addition to the methonium compounds, he has worked on diving physiology and caisson disease, on histamine and its release, and on synaptic transmission. From 1951 to 1956 he was secretary of the Physiological Society, and was elected F.R.S. in 1956.

University of Cambridge

On Feb. 21 the following degrees were conferred:

M.A.—J. H. Cullen.
M.B.—W. E. I. Forsythe-Jauch.

Order of St. John

On March 5 two foundation stones of the Order's new ophthalmic hospital in Jerusalem were to be laid, one inscribed in English and the other in Arabic. The first was to be laid by Lieut.-General Sir Henry Pownall, the chancellor of the Order, and the second by Sir Stewart Duke-Elder, the hospitaller. The warden's house and nurses' quarters are already finished, and it is expected that the main hospital building will be completed by the early autumn of next year.

Arthur Hall Lecture

On Friday, April 3, at 8.15 P.M., at the University of Sheffield, Western Bank, Lord Kilmuir will give an Arthur Hall lecture. His subject will be medicine and the law.

Institute of Almoners

The annual general meeting of this institute will be held on Friday, March 20, at 6 P.M., at the Fishmongers' Hall, London Bridge, E.C.4. Mr. R. Huws Jones will give an address entitled Is Our Social Worker Really Necessary?

Principles, Methods, and Media of Health Education

The Central Council for Health Education will hold an international seminar on this subject from April 21 to 24 at the London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1. Further particulars may be had from the medical director of the Council, Tavistock House, W.C.1.

Nursing and Health Exhibition

The London County Council and the four Metropolitan Regional Hospital Boards are holding an exhibition at County Hall, Westminster Bridge, S.E.1, to show (1) what is being done for the health of the people of London after ten years of the National Health Service, and (2) what opportunities there are in nursing and the allied professions. It will be open daily (except Sunday) from 10 A.M. to 8 P.M. until March 14.

Mr. E. A. Nicoll is leaving on March 6 for Rio de Janeiro where he will lecture on orthopædic surgery at the invitation of the Brazilian Government. Later he will visit Uruguay under the auspices of the British Council. He returns on March 30.

CORRIGENDUM: " *Protein-losing Gastroenteropathy* ".—In this leading article (Feb. 14, p. 351) we said that the turnover-rate of serum-albumin in man was measured by means of ^{131}I-labelled albumin in 1949. In fact this technique was first described in 1951 by K. Sterling (*J. clin. Invest.* 1951, **30**, 1228, 1238). The paper by R. S. Gordon cited in footnote 9 did not, as we implied, deal with clinical results.

he Royal
d to the
urn. He

s honours
studies at
and after
unit there
III Sana-
er of the
Institute
rk on the
aimis, he
dinburgh,
Toronto.
t Univer-
g year he
st holder,
s worked
and its
6 he was
in 1956.

er's new
cribed in
laid by
of the
der, the
ters are
hospital
t year.

ersity of
Arthur
w.

be held
rs' Hall,
give an
ry?

cation

hold an
to 24 at
, Keppel
ad from
, W.C.1.

opolitan
County
is being
years of
ies there
be open
ch 14.

where he
Brazilian
ces of the

-In this
er-rate of
I-labelled
d in 1951
paper by
deal with